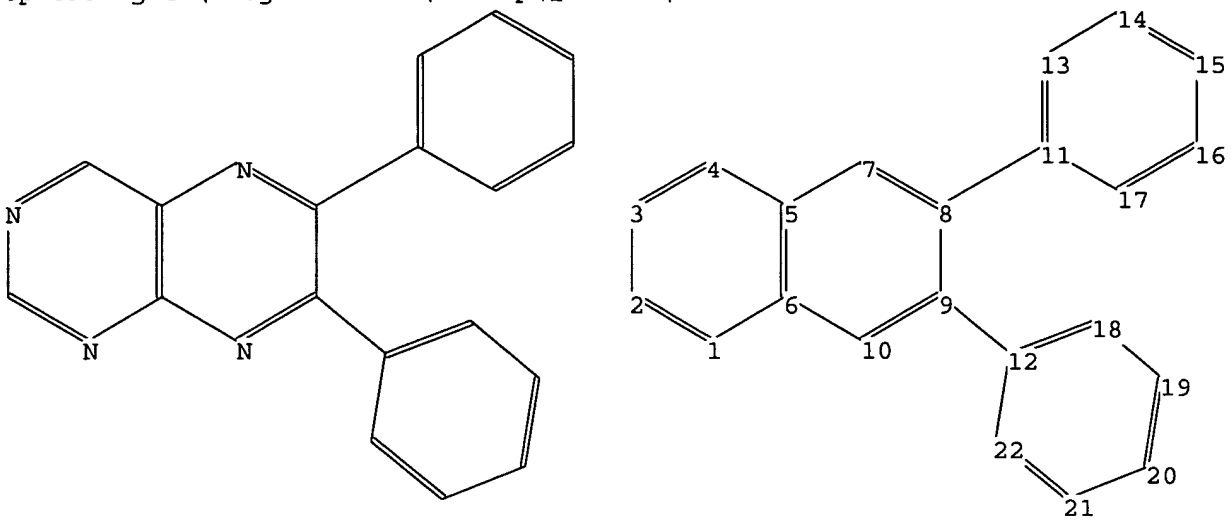
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10679209.str



ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
chain bonds :
8-11 9-12
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-13 11-17 12-18 12-22
13-14 14-15 15-16 16-17 18-19 19-20 20-21 21-22
exact bonds :
8-11 9-12
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-13 11-17 12-18 12-22
13-14 14-15 15-16 16-17 18-19 19-20 20-21 21-22
isolated ring systems :
containing 11 : 12 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom

L1 STRUCTURE UPLOADED

=> ld
LD IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

```
=> d
L1 HAS NO ANSWERS
L1              STR
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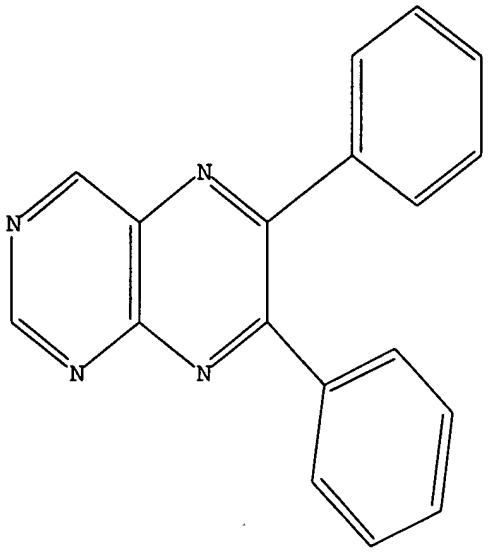


```
Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 08:45:26 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       45 TO ITERATE

100.0% PROCESSED       45 ITERATIONS                                16 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          498 TO     1302
PROJECTED ANSWERS:              80 TO      560

L2            16 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 08:45:33 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     1016 TO ITERATE

100.0% PROCESSED     1016 ITERATIONS                              344 ANSWERS
SEARCH TIME: 00.00.01

L3           344 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                 166.94     167.15

FILE 'CAPLUS' ENTERED AT 08:45:40 ON 30 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
```

FILE COVERS 1907 - 30 May 2006 VOL 144 ISS 23
FILE LAST UPDATED: 28 May 2006 (20060528/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4 181 L3

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.92	168.07

FILE 'REGISTRY' ENTERED AT 08:47:06 ON 30 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 MAY 2006 HIGHEST RN 885861-83-6
DICTIONARY FILE UPDATES: 28 MAY 2006 HIGHEST RN 885861-83-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

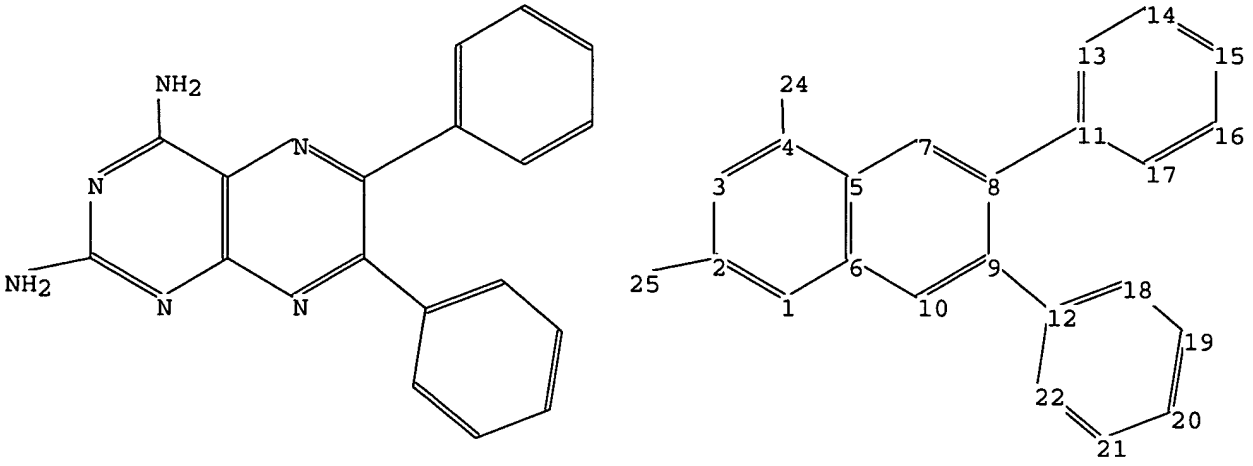
****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\106792092.str



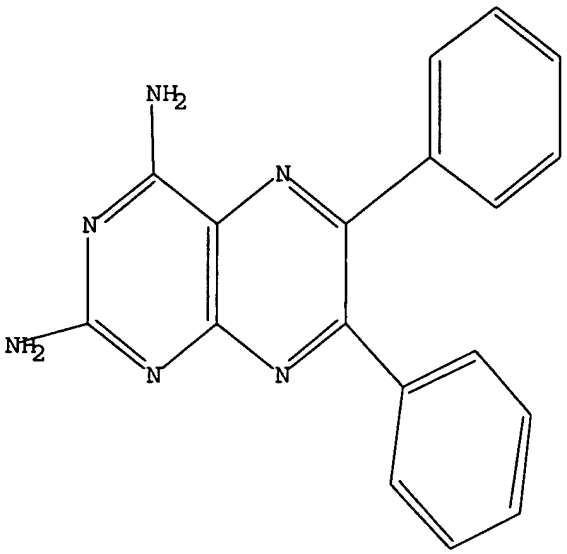
chain nodes :
24 25
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
chain bonds :
2-25 4-24 8-11 9-12
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-13 11-17 12-18 12-22
13-14 14-15 15-16 16-17 18-19 19-20 20-21 21-22
exact/norm bonds :
2-25 4-24
exact bonds :
8-11 9-12
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-13 11-17 12-18 12-22
13-14 14-15 15-16 16-17 18-19 19-20 20-21 21-22
isolated ring systems :
containing 11 : 12 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 24:CLASS 25:CLASS

L5 STRUCTURE UPLOADED

=> d

L5 HAS NO ANSWERS
L5 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l5
SAMPLE SEARCH INITIATED 08:47:23 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 4 TO 200
PROJECTED ANSWERS: 0 TO 0

L6 0 SEA SSS SAM L5

=> s l5 full
FULL SEARCH INITIATED 08:47:32 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 103 TO ITERATE

100.0% PROCESSED 103 ITERATIONS 25 ANSWERS
SEARCH TIME: 00.00.01

L7 25 SEA SSS FUL L5

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 166.94 335.01

FILE 'CAPLUS' ENTERED AT 08:47:38 ON 30 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

10679209 5/25/06

FILE COVERS 1907 - 30 May 2006 VOL 144 ISS 23
FILE LAST UPDATED: 28 May 2006 (20060528/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

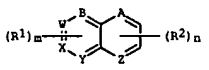
=> s l7
L8 45 L7

=> d ibib abs hitstr tot

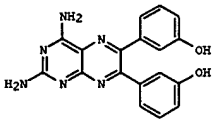
L8 ANSWER 1 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1335074 CAPLUS
DOCUMENT NUMBER: 144:69859
TITLE: Indoles, pteridines, pyridopyrazines, and benzotriazines as vasculostatic agents, their preparation, pharmaceutical compositions and use in therapy
INVENTOR(S): Wrasidlo, Wolfgang; Doukas, John; Royston, Ivor; Noronha, Glenn; Hood, John D.; Dneprovskaia, Elena; Gong, Xianchang; Splittgerber, Ute; Zhao, Ningning
PATENT ASSIGNEE(S): Targegen, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 95 pp., Cont.-in-part of U.S. Ser. No. 679,209.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005282814	A1	20051222	US 2005-105845		20050413
US 2004167198	A1	20040826	US 2003-679209		20031002
PRIORITY APPLN. INFO.:			US 2003-679209		20031002
			US 2002-415981P	P	20021003
			US 2003-440234P	P	20030114
			US 2003-443752P	P	20030129
			US 2003-463818P	P	20030417
			US 2003-466983P	P	20030430
			US 2003-479295P	P	20030617
			US 2003-679209	A2	20031002

OTHER SOURCE(S): MARPAT 144:69859
GI

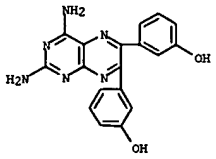


I



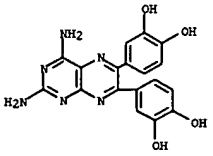
II

L8 ANSWER 1 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
AB The invention relates to nitrogen heterocyclic compds. of formula I, which are useful for treating disorders associated with compromised vasculostasis. In compds. I, each of A, B, W, X, Y, and Z is independently selected from C, C(O), N, and NR3, where R3 is H or (un)substituted alkyl; each R1 is independently halo, OR4, N(R4)2, or SR4, where R4 is H, lower alkyl, aryl, heteroaryl, etc.; each R2 is independently halo, OR5, N(R5)2, SR5, OPO3H2, (un)substituted alkyl, (un)substituted aryl, (un)substituted heteroaryl, where R5 is H, lower alkyl, aryl, heteroaryl, etc.; and each of m and n is independently an integer from 1 to 4. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. for the treatment of a variety of disorders including stroke, myocardial infarction, cancer, ischemia/reperfusion injury, autoimmune diseases such as rheumatoid arthritis, eye diseases such as retinopathies or macular degeneration, inflammatory diseases, vascular leakage syndrome, edema, transplant rejection, adult/acute respiratory distress syndrome (ARDS), and the like. Cyclocondensation of 3,3'-dihydroxybenzil with 2,4,5,6-tetraaminopyrimidine sulfate results in the formation of diaminopteridine II. Compound II expresses an IC50 value of 83 nM in an assay for the inhibition of the human p120γ subunit of PI3 kinase and results in 65% reduction of myocardial infarction in rats.
IT **677297-51-7P**, 6,7-Bis(3-hydroxyphenyl)pteridine-2,4,-diamine **677297-63-1P**, 6,7-Bis(3,4-dihydroxyphenyl)pteridine-2,4-diamine dihydrochloride
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of vasculostatic agents and use for treatment
of disorders associated with compromised vasculostasis)
RN 677297-51-7 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis- (9CI) (CA INDEX NAME)



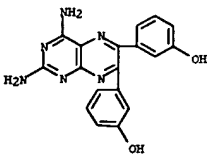
RN 677297-63-1 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,4-diamino-6,7-pteridinediyl)bis-, dihydrochloride (9CI) (CA INDEX NAME)

L8 ANSWER 1 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



●2 HCl

IT **677297-55-1P**, 6,7-Bis(3-hydroxyphenyl)pteridine-2,4-diamine dihydrochloride **677297-56-2P**, 6,7-Bis(3-hydroxyphenyl)pteridine-2,4-diamine methanesulfonate **677297-57-3P**, 6,7-Bis(3-hydroxyphenyl)pteridine-2,4-diamine dihydrobromide **677297-62-0P**, 6,7-Bis(3,4-dihydroxyphenyl)pteridine-2,4-diamine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of vasculostatic agents and use for treatment
of disorders associated with compromised vasculostasis)
RN 677297-55-1 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis-, dihydrochloride (9CI) (CA INDEX NAME)



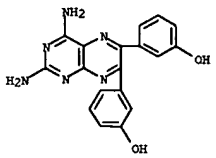
●2 HCl

RN 677297-56-2 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis-, methanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 677297-51-7
CMF C18 H14 N6 O2

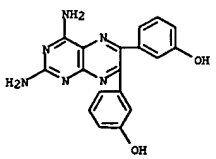
L8 ANSWER 1 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

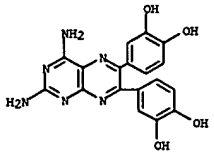
RN 677297-57-3 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis-, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

RN 677297-62-0 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,4-diamino-6,7-pteridinediyl)bis- (9CI) (CA INDEX NAME)

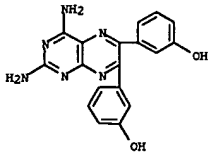
L8 ANSWER 1 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



IT 677298-35-0, 6,7-Bis-(3-hydroxyphenyl)pteridine-2,4-diamine sulfate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of vasculostatic agents and use for treatment of disorders associated with compromised vasculostasis)
RN 677298-35-0 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis-, sulfate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 677297-51-7
CMF C18 H14 N6 O2



CM 2

CRN 7664-93-9
CMF H2 O4 S

L8 ANSWER 1 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L8 ANSWER 2 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:308364 CAPLUS
DOCUMENT NUMBER: 140:321386
TITLE: Preparation of vasculostatic agents and methods of use
INVENTOR(S): Wrasidlo, Wolfgang; Doukas, John; Royston, Ivor; Noronha, Glenn; Hood, John D.; Dneprovskaia, Elena; Gong, Xianchang; Splittgerber, Ute; Zhao, Ningning
PATENT ASSIGNEE(S): Targegen, Inc., USA
SOURCE: PCT Int. Appl., 230 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004030635	A2	20040415	WO 2003-US31721	20031002
WO 2004030635	A3	20040812		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2500727	AA	20040415	CA 2003-2500727	20031002
AU 2003282726	A1	20040423	AU 2003-282726	20031002
EP 1549614	A2	20050706	EP 2003-774610	20031002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015053	A	20050809	BR 2003-15053	20031002
CN 1720224	A	20060111	CN 2003-80104711	20031002
JP 2006515317	T2	20060525	JP 2005-500378	20031002

PRIORITY APPLN. INFO.: US 2002-415981P P 20021003
US 2003-440234P P 20030114
US 2003-443752P P 20030129
US 2003-463818P P 20030417
US 2003-466983P P 20030430
US 2003-479295P P 20030617
WO 2003-US31721 W 20031002

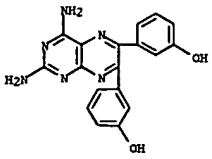
OTHER SOURCE(S): MARPAT 140:321386
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

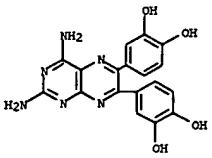
AB Compds. (2 Markush structures shown as I and II; others are described in the claims and disclosure; variables defined below; e.g. III and IV) and methods are provided for treating disorders associated with compromised vasculostasis. Invention methods and compns. are useful for treating a variety of disorders including for example, stroke, myocardial infarction, cancer, ischemia/reperfusion injury, autoimmune diseases such as rheumatoid arthritis, eye diseases such as retinopathies or macular degeneration or other vitreoretinal diseases, inflammatory diseases,

L8 ANSWER 2 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
vascular leakage syndrome, edema, transplant rejection, adult/acute respiratory distress syndrome (ARDS), and the like. Although the methods of prepn. are not claimed, many example prepns. are included. For example, III was prepd. (75 %) from 2-(2-aminophenyl)indole and 4-hydroxyphenylacetic acid. Various expts. are described that show the use of the claimed compds. along with chemotherapeutic agents for cancer treatment. The claimed compds. also show inhibition of vascular leak induced by interleukin 2. Inhibition of VEGF-induced edema, redn. of myocardial infarction and inhibition of c-Src and Yes kinases were demonstrated for some of the claimed compds. For I: each R0 = -H, -COOH, -OR', -SO3H, wherein R' is - H or lower alkyl, or when x = 2, each R0 is taken together to form a 1,3-dioxolyl ring, or each R0 = (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted cycloalkyl, (un)substituted heterocyclic, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted alkylaryl, (un)substituted arylalkyl, (un)substituted arylalkenyl, (un)substituted arylalkynyl, halogen, amino, amido, nitro, or thioalkyl. R1 and R2 = H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted cycloalkyl, (un)substituted heterocyclic, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted alkylaryl, (un)substituted arylalkyl, (un)substituted arylalkenyl, (un)substituted arylalkynyl; G is NH, O, S, or (CR'')p, wherein R'' is -H, lower alkyl, or acetamido, and wherein p = 0-3; Ar is aryl or heteroaryl, and x and y = 1-4. For II: Z1-Z6 = C, -C:O, N, or NRa, wherein Ra is -H, (un)substituted alkyl, wherein said substituents are halogen, hydroxy, oxo, or amino; each X = halogen, -ORb, -NRb2, or -SRb, wherein Rb is -H lower alkyl, -(CH2)2NHEt, -(CH2)3morpholin-1-yl, -(CH2)3-(N-methylpiperazin-1-yl), aryl, heteroaryl, -(NH-NH-Rc), -(N:N-NH-Rc), wherein Rc is H or lower alkyl. Each Y = -ORd, -NRd2, -SRd, or -OPO3H2 wherein Rd is H, lower alkyl, aryl, heteroaryl, -(CH2)2NHEt, -(CH2)3morpholin-1-yl, or (CH2)3-(N-methylpiperazin-1-yl); or each Y = (un)substituted alkyl, (un)substituted aryl, (un)substituted heteroaryl, or halogen, wherein said substituents = halogen, -ORe, -NRe2, -SRe, -P(O)(OH)2, wherein Re is -H, lower alkyl, aryl, or heteroaryl; or each Y = CH2glycinyl, CH2NHethoxy, CH2NHCH2alkyl, CH2NHCH2t-Bu, CH2NHCH2aryl, CH2NHCH2substituted aryl, CH2NHCH2heteroaryl, CH2NHCH2substituted heteroaryl; or when n is 2, each Y is taken together to form a fused arom. or heteroarom. ring system; and m and n = 1 to 4, wherein when Z1, Z3, Z5, and Z6 are each N, X is NH2, and m = n = 2, Y is not Ph or 4-hydroxyphenyl.
IT 677297-51-7P, 6,7-Bis(3-hydroxyphenyl)pteridine-2,4-diamine
677297-63-1P, 6,7-Bis(3,4-dihydroxyphenyl)pteridine-2,4-diamine dihydrochloride
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of vasculostatic agents and methods of use)
RN 677297-51-7 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis- (9CI) (CA INDEX NAME)

L8 ANSWER 2 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



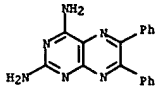
RN 677297-63-1 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,4-diamino-6,7-pteridinediyl)bis-, dihydrochloride (9CI) (CA INDEX NAME)



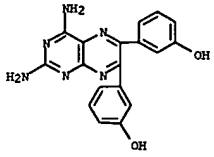
●2 HCl

IT 18181-93-6P, 6,7-Diphenylpteridine-2,4-diamine
677297-50-6P, 6,7-Bis(3-hydroxyphenyl)pteridine-2,4-diamine monohydrochloride 677297-55-1P, 6,7-Bis(3-hydroxyphenyl)pteridine-2,4-diamine dihydrochloride 677297-56-2P, 6,7-Bis(3-hydroxyphenyl)pteridine-2,4-diamine methanesulfonate 677297-57-3P, 6,7-Bis(3-hydroxyphenyl)pteridine-2,4-diamine dihydrobromide 677297-62-0P, 6,7-Bis(3,4-dihydroxyphenyl)pteridine-2,4-diamine 677298-35-0P, 6,7-Bis(3-hydroxyphenyl)pteridine-2,4-diamine sulfate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of vasculostatic agents and methods of use)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

L8 ANSWER 2 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

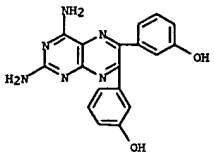


RN 677297-50-6 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 677297-55-1 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis-, dihydrochloride (9CI) (CA INDEX NAME)



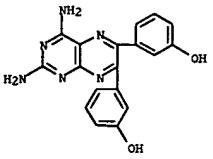
●2 HCl

RN 677297-56-2 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis-, methanesulfonate (salt)

L8 ANSWER 2 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

CM 1

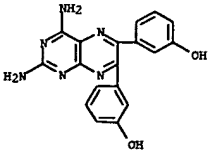
CRN 677297-51-7
CMF C18 H14 N6 O2



CM 2

CRN 75-75-2
CMF C H4 O3 S

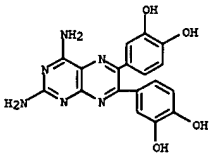
RN 677297-57-3 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis-, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

RN 677297-62-0 CAPLUS
CN 1,2-Benzenediol, 4,4'-(2,4-diamino-6,7-pteridinediyl)bis- (9CI) (CA INDEX

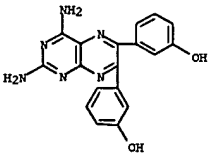
L8 ANSWER 2 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
NAME)



RN 677298-35-0 CAPLUS
CN Phenol, 3,3'-(2,4-diamino-6,7-pteridinediyl)bis-, sulfate (salt) (9CI) (CA INDEX NAME)

CM 1

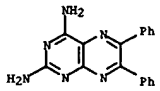
CRN 677297-51-7
CMF C18 H14 N6 O2



CM 2

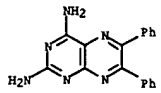
CRN 7664-93-9
CMF H2 O4 S

L8 ANSWER 3 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:758726 CAPLUS
DOCUMENT NUMBER: 140:314320
TITLE: Determination of lipophilic descriptors of antihelmintic 6,7-diaryl-pteridine derivatives useful for bioactivity predictions
AUTHOR(S): Reta, Mario; Giacomelli, Liliana; Santo, Marisa; Cattana, Rosa; Silber, Juana J.; Ochoa, Carmen; Rodriguez, Mercedes; Chana, Antonia
CORPORATE SOURCE: Departamento de Quimica, Universidad Nacional de Rio Cuarto, Rio Cuarto, 5800, Argent.
SOURCE: Biomedical Chromatography (2003), 17(6), 365-372
CODEN: BICHE2; ISSN: 0269-3879
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The liquid chromatog. retention factors extrapolated to pure water, k'w, for several 6,7-diaryl-pteridine derivs. in both an octadecylsilane (ODS) and an immobilized artificial membrane column (IAM.PC.DD2), using acetonitrile-aqueous buffer pH = 7.45 as mobile phase, were obtained. The logarithms of the k'w values in the IAM.PC.DD2 column, log k'IAMw, show good correlation with the calculated values of the octanol-water partition coeffs., log Po/w, showing that the chromatog. parameter can be used as lipophilicity descriptor for the studied pteridines. However, interactions other than the lipophilic ones seem to be involved in the ODS column. Previous studies have shown that pteridines have antihelmintic properties. In spite of the complexity of the studied biol. system as compared with the chromatog. one, good correlation between the descriptors obtained in the IAM column and biol. activity (expressed as the log of the inhibitory concentration required to obtain up to 50% in the reduction of population
growth of nematodes, log IC50) was observed
IT 18181-93-6
RL: ANT (Analyte); BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(determination of lipophilic descriptors of antihelmintic 6,7-diaryl-pteridine
derivs. for bioactivity predictions)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

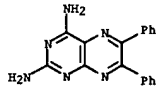
L8 ANSWER 4 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:125984 CAPLUS
DOCUMENT NUMBER: 138:368664
TITLE: Pteridines. Part CXIII. Protection of pteridines
AUTHOR(S): Yao, Qizineng; Pfleiderer, Wolfgang
CORPORATE SOURCE: Fachbereich Chemie, Universitaet Konstanz, Konstanz, D-78457, Germany
SOURCE: Helvetica Chimica Acta (2003), 86(1), 1-12
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:368664
AB The low solubility of pterins can drastically be improved by N2-acylation or formation of the N2-[(dimethylamino)methylene] derivs. Both types of compds. can be alkylated under Mitsunobu conditions to form N2-acylpterins and their derivs. N2,N2-Dimethylpterins and N2-methylpterins direct alkylation to the O4-position. Deacylation can be achieved under very mild conditions by solvolysis with MeOH, and displacement of the O4-[2-(4-nitrophenyl)ethyl] group proceeds with ammonia at room temperature to
the corresponding pteridin-2,4-diamines. Cleavage of the N2[(dimethylamino)methylene] group works well with ammonia. The advantage of applying the 2-(4-nitrophenyl)ethyl (npe) group as blocking group is seen in its selective removal by 1.8-diazabicyclo[5.4.0]undec-7-ene (DBU) under aprotic conditions without harming the other substituents.
IT 18181-93-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(N2-acylation of pterins followed by Mitsunobu alkylation to form alkyl derivs. of pterins)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

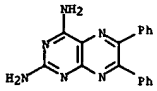
L8 ANSWER 5 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:589097 CAPLUS
DOCUMENT NUMBER: 131:317316
TITLE: Inhibition of Neuronal Nitric Oxide Synthase by 4-Amino Pteridine Derivatives: Structure-Activity Relationship of Antagonists of (6R)-5,6,7,8-Tetrahydrobiopterin Cofactor
AUTHOR(S): Froehlich, Lothar G.; Kotsonis, Peter; Traub, Hermann; Taghavi-Moghadam, Shahriyar; Al-Masoudi, Najim; Hofmann, Heinrich; Strobel, Hartmut; Matter, Hans; Pfleiderer, Wolfgang; Schmidt, Harald H. H. W.
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Julius-Maximilians University Wuerzburg, Wuerzburg, 97078, Germany
SOURCE: Journal of Medicinal Chemistry (1999), 42(20), 4108-4121
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The family of nitric oxide synthases (NOS) catalyzes the conversion of L-arginine to L-citrulline and nitric oxide (NO), an important cellular messenger mol. which has been implicated in the pathophysiol. of septic shock and inflammatory and neurodegenerative disease states. NOS can be maximally activated by the ubiquitous cofactor, (6R)-5,6,7,8-tetrahydrobiopterin (H4Bip), and antagonists of H4Bip may be of therapeutic importance to inhibit pathol. high NO formation. The 4-amino substituted analog of H4Bip was reported to be a potent NOS inhibitor. Therefore, we developed a series of novel 4-amino pteridine derivs., anti-pterins, to pharmacol. target the neuronal isoform of nitric oxide synthase (NOS-I). To functionally characterize the pterin/anti-pterin interaction and establish a structure-activity relationship (SAR), we systematically altered the substituents in the 2-, 4-, 5-, 6-, and 7-position of the pteridine nucleus. Varying the substitution pattern in the 2-, 5-, and 7-position resulted in no significant inhibitory effect on enzyme activity. In contrast, bulky substituents in the 6-position, such as Ph, markedly increased the inhibitory potency of the reduced 4-amino-5,6,7,8-tetrahydropteridines, possibly as a consequence of hydrophobic interactions within NOS-I. However, this was not the case for the aromatic 4-amino pteridines. Interestingly, chemical modification of the 4-amino substituent by dialkyl/diaralkylation together with 6-arylation of the aromatic 2,4-diamino pteridine resulted in potent and efficacious inhibitors of NOS-I, suggesting possible hydrophilic and hydrophobic interactions within NOS-I. This SAR agrees with (a) the recently published crystal structure of the oxygenase domain of the inducible NOS isoform (NOS-II) and (b) the comparative mol. field anal. of selected NOS-I inhibitors, which resulted in a 3D-QSAR model of the pterin binding site interactions. Further optimization should be possible when the full length structure of NOS-I becomes available.
IT 18181-93-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of and inhibition of neuronal nitric oxide synthase by aminopteridines)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

L8 ANSWER 5 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



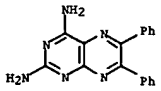
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:237746 CAPLUS
DOCUMENT NUMBER: 128:291449
TITLE: Application of neural networks to the study of structure-activity relationships of 6,7-diarylpteridines as nematocides
AUTHOR(S): Ochoa, C.; Rodriguez, J.; Rodriguez, M.; Chana, A.; Stud, M.; Alonso-Villalobos, P.; Martinez-Grueiro, M. M.
CORPORATE SOURCE: Inst. Quimica Medica, Madrid, 28006, Spain
SOURCE: Medicinal Chemistry Research (1997), 7(9), 530-545
CODEN: MCREEB; ISSN: 1054-2523
PUBLISHER: Birkhaeuser Boston
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A study of structure-activity relationships of 6,7-diarylpteridines as nematocides, using a trained back-propagation neural network, has been carried out. This network has allowed the prediction of the qual. nematocide activity of pteridine derivs. not yet synthesized. Among 25 preselected pteridine derivs., 17 were predicted as nematocides by the network. The synthesis and the nematocidal activity of the pteridines, which had been predicted as active compds., are reported. Use of this network allows the prediction of qual. nematocide activity of pteridine derivs., not yet synthesized.
IT 18181-93-6
RL: AGR (Agricultural use); BIOL (Biological study); USES (Uses)
(neural network simulation for prediction of nematocidal activity)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

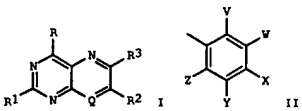
L8 ANSWER 7 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:466654 CAPLUS
DOCUMENT NUMBER: 125:157774
TITLE: Anthelmintic activity of 6,7-diarylpteridines
AUTHOR(S): Ochoa, Carmen; Rodriguez, Juan; Lopez Garcia, Maria Luz; Martinez, Antonio Ramon; Martinez, Maria Mercedes
CORPORATE SOURCE: Fac. Farm., Univ. Complutense, Madrid, E-28006, Spain
SOURCE: Arzneimittel-Forschung (1996), 46(6), 643-648
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Cantor
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In search for new anthelmintic compds., some 6,7-diaryl-pteridines were synthesized from the corresponding diaminopyrimidines and aromatic aldehydes.
Their anthelmintic activity was tested in vitro against Caenorhabditis elegans and Heligmosomoides polygyrus and in vivo against Trichinella spiralis. Structure-activity relationships are discussed.
IT 18181-93-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(anthelmintic activity and preparation of diarylpteridines)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 8 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:324866 CAPLUS
DOCUMENT NUMBER: 122:258655
TITLE: Preparation of insecticidal pteridines and 8-deazapteridines.
INVENTOR(S): Henrie, Robert Neil, II; Peake, Clinton Joseph; Cullen, Thomas Gerard; Lew, Albert Chieh; Silverman, Ian Robert
PATENT ASSIGNEE(S): FMC Corp., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

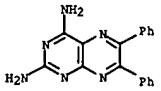
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9427439	A1	19941208	WO 1994-US4474	19940425
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5521190	A	19960528	US 1993-67897	19930527
AU 9467726	A1	19941220	AU 1994-67726	19940425
US 5532367	A	19960702	US 1995-416017	19950331
US 5639753	A	19970617	US 1995-612657	19951128
PRIORITY APPLN. INFO.:			US 1993-67897 A	19930527
			WO 1994-US4474 W	19940425

OTHER SOURCE(S): MARPAT 122:258655
GI

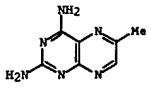


AB Pteridine and 8-deazapteridine compds. and compns. were prepared and used for controlling insects in agricultural crops. These pteridines may be represented by structure [I, R and R1 = NH2, lower alkylamino, di(lower alkyl)amino (e.,g., NMe2), or di(lower alkyl)aminomethyleneamine (e.g., N=CHNMe2); R2 = H, NH2, lower alkyl (e.g., -CH3, -CH(CH3)2), di(lower alkyl)aminomethyleneamino, OH, lower alkoxy, Ph or substituted Ph, haloalkylphenylalkyl (e.g., 3-trifluoromethylphenylmethyl); Q = N or CH; R3 = (n)m-R4, m = 0 or 1; when m = 1, n is a bridging atom or moiety selected from O, S, SO, SO2, lower alkylene (e.g., CH2 or CH2CH2), lower alkenylene (e.g., CH=CH), lower alkynylene (e.g., C.tplbond.C), lower haloalkenylene (e.g., C(Cl)=CH), CO, aminomethyl (e.g., CH2NH), or (substituted amino)methyl (e.g., CH2NMe); and R4 = H, lower alkyl (e.g., Me, i-Pr), thien-2-yl, pyridin-3-yl, or II; V, W, X, Y = H, halo, haloalkyl, aryl, Ph, PhO; Z = H or halo]. A typical dust formulation against tobacco budworm contained 1 part 2,4-diamino-6-[3,5-di(trifluoromethyl)phenyl]-7-methylpteridine and 99 parts talc.

L8 ANSWER 8 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
IT 18181-93-6P
RL: AGR (Agricultural use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and insecticidal activity of pteridine derivs.)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 9 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:134419 CAPLUS
DOCUMENT NUMBER: 120:134419
TITLE: Protection and deprotection of fused 2-amino-4(3H)-pyrimidinones: conversion of pterins and 5-deazapterins to 2,4-diamino derivatives
AUTHOR(S): Taylor, Edward C.; Otiv, S. R.; Durucasu, Inci
CORPORATE SOURCE: Dep. Chem., Princeton Univ., Princeton, NJ, 08544, USA
SOURCE: Heterocycles (1993), 36(8), 1883-95
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:134419
GI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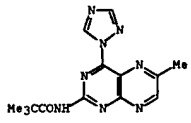
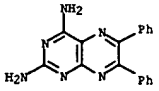

II

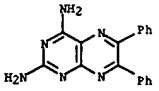
AB 5-Deazapterins and pterins are readily converted to their 4-deoxy-4-amino derivs., e.g. I, (a lactam-to-amidine conversion) by reaction with 4-chlorophenyl phosphorodichloridate and 1,2,4-triazole to give intermediate 4-[1'-(1,2,4-triazolyl)] derivs., e.g. II, followed by reaction with aqueous ammonia. Some anomalous results obtained by application of the Mitsunobu reaction (normally a lactam-to-lactim ether conversion) to 5-deazapterins are detailed.

IT 18181-93-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

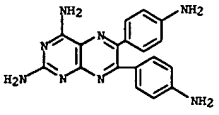
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 10 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



RN 151648-52-1 CAPLUS
CN 2,4-Pteridinediamine, 6,7-bis(4-aminophenyl)- (9CI) (CA INDEX NAME)

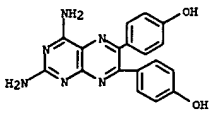


L8 ANSWER 10 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:4377 CAPLUS
DOCUMENT NUMBER: 120:4377
TITLE: Identification of highly potent and selective inhibitors of Toxoplasma gondii dihydrofolate reductase
AUTHOR(S): Chio, Li Chun; Queener, Sherry F.
CORPORATE SOURCE: Sch. Med., Indiana Univ., Indianapolis, IN, 46202-5120, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1993), 37(9), 1914-23
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

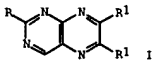
AB Toxoplasma gondii RH was obtained in high yield from culture in RPMI medium on a line of Chinese hamster ovary cells lacking dihydrofolate reductase activity (ATCC 3952 dhfr-). Dihydrofolate reductase prepns. from harvested organisms had sp. activities of 22.9 nmol/min/mg. The 50% inhibitory concns. against reference compds. were 0.014 μM for methotrexate, 0.25 μM for pyrimethamine, 2.7 μM for trimethoprim, and 0.010 μM for trimetrexate. The Km value for NADPH was 11 μM and followed Michaelis-Menten kinetics; the Km for dihydrofolate was .apprx.11 μM, but substrate inhibition appeared to occur at high substrate concns. Dihydrofolate reductase from T. gondii was used to screen 130 compds. from the National Cancer Institute repository. Thirteen compds. were >100-fold more potent than pyrimethamine toward T. gondii dihydrofolate reductase; 6 compds. with various potencies were 8-46 times as selective as pyrimethamine for the protozoal form of the enzyme over the mammalian form. Four trimetrexate analogs were more potent than trimetrexate, and 2 were significantly more selective. Representative compds. were also tested in a culture model of T. gondii employing uracil incorporation as an index of growth. One pyrimethamine analog was as effective as pyrimethamine in inhibiting T. gondii in culture (50% inhibitory concentration, 0.45 μM). Three other compds. were also effective at micromolar concns.

IT 6967-77-7 18181-93-6 151648-52-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dihydrofolate reductase of Toxoplasma gondii inhibition by, structure in relation to)

RN 6967-77-7 CAPLUS
CN Phenol, 4,4'-(2,4-diamino-6,7-pteridinediyl)bis- (9CI) (CA INDEX NAME)



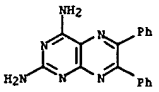
L8 ANSWER 11 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:164728 CAPLUS
DOCUMENT NUMBER: 84:164728
TITLE: Direct conversion of 4-hydroxypteridines to their 4-amino analogs
AUTHOR(S): Gapski, G. R.; Whiteley, J. M.
CORPORATE SOURCE: Scripps Clin. Res. Found., La Jolla, CA, USA
SOURCE: Chem. Biol. Pteridines, Proc. Int. Symp., 5th (1975), 627-32. Editor(s): Pfleiderer, Wolfgang. de Gruyter: Berlin, Ger.
CODEN: 32LMAC
DOCUMENT TYPE: Conference
LANGUAGE: English
GI


I

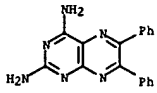
AB The 4-aminopteridines I (R = NH2, R1 = H, Me, Ph) were prepared in 27-42% yields by treating I (R = OH) with PhOP(O)(NH2)2.

IT 18181-93-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation by amination of hydroxypteridines with phenylphosphorodiamidate)

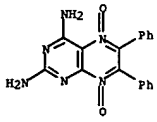
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



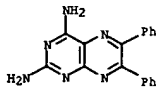
L8 ANSWER 12 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1974:37071 CAPLUS
DOCUMENT NUMBER: 80:37071
TITLE: Pteridines. LVIII. Synthesis and properties of pterin and 2,4-diaminopteridine mono- and di-N-oxides
AUTHOR(S): Yamamoto, Hiroshi; Hutzenlaub, Wolfgang; Pfleiderer, Wolfgang
CORPORATE SOURCE: Fachbereich Chem., Univ. Konstanz, Constance, Fed. Rep. Ger.
SOURCE: Chemische Berichte (1973), 106(10), 3175-93
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB Treating pterins (I; n = m = 0; R, R1 = H, Me, or Ph) and diaminopteridines (II, n = m = 0) with H2O2-CF3CO2H gave preferentially the oxides I and II (n = 1, m = 0, and n = m = 1), the structures of which were proven by rearrangement, hydrolysis, and uv spectra. I (m = n = 0, R = H, R1 = CMe3 and Ph) were oxidized to give the 5-oxides I (m = 1, n = 0) due to steric hindrance. The pKa values and uv spectra are discussed.
IT **18181-93-6P 51324-31-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



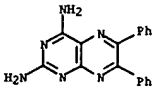
RN 51324-31-3 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl-, 5,8-dioxide (9CI) (CA INDEX NAME)



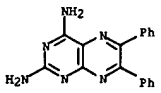
L8 ANSWER 13 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:446130 CAPLUS
DOCUMENT NUMBER: 71:46130
TITLE: Dihydrofolate reductase from Trypanosoma equiperdum. II. Inhibition by 2,4-diaminopyrimidines and related heterocycles
AUTHOR(S): McCormack, John J., Jr.; Jaffe, Julian J.
CORPORATE SOURCE: Coll. of Med., Univ. of Vermont, Burlington, VT, USA
SOURCE: Journal of Medicinal Chemistry (1969), 12, 662-8
CODEN: JMCHAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A number of 2,4-diaminopyrimidines and related heterocyclic compds. have been evaluated as inhibitors of dihydrofolate reductase obtained from T. equiperdum, chicken liver, and rat liver. 2,4-Diaminopyrimidine itself (at 10-4M) was not effective as an inhibitor of dihydrofolate reduction in all 3 systems studied but 5-aryl derivs. of 2,4-diaminopyrimidine were good in-inhibitors (ID50 = 10-8 to 10-6M) of this enzymic reaction. 2,4-Diamino-5-benzylpyrimidines and 2,4-diamino-5-aryloxypyrimidines were considerably more effective as inhibitors of the trypanosomal enzyme system than of the mammalian and avian systems. Although 2,4-diamino-6-phenyl-s-triazine was not active as an inhibitor of the enzymes studied, related 4,6-diamino-1,2-dihydro-s-triazines were potent inhibitors of the reductases. 2,4-Diamino-6,7-diphenylpteridine was found to be approx. 10-fold more effective as an inhibitor of the 3 reductase systems than was 2,4-diamino-6,7-dimethylpteridine; 2-amino-6,7-diphenylpteridine and 4-amino-6,7-diphenylpteridine were not effective as inhibitors of these enzymes. 2,4,7-Triamino-6-arylpteridines bearing an ortho substituent in the 6-aryl moiety were 10-100-fold more potent as inhibitors of the reductase systems than were the corresponding para-substituted derivs. The 2-amino-4-hydroxypteridine derivs. biopterin, xanthopterin, and isoxanthopterin were effective neither as substrates nor as inhibitors of the trypanosomal reductase.
IT **18181-93-6**
RL: BIOL (Biological study)
(tetrahydrofolate dehydrogenase response to)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 14 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:458202 CAPLUS
DOCUMENT NUMBER: 69:58202
TITLE: Stimulation by pteridines of the uptake of amethopterin by human lymphocytes
AUTHOR(S): Kessel, David; Botterill, Vivienne; Hall, Thomas C.
CORPORATE SOURCE: Lab. of Pharmacol., Children's Cancer Res. Found., Boston, MA, USA
SOURCE: Biochemical Pharmacology (1968), 17(8), 1727-33
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Triamterene (2,4,7-triamino-6-phenylpteridine) and certain other pteridines stimulated the uptake of amethopterin by human small lymphocytes, apparently by removing a barrier to amethopterin transport. This stimulation did not extend appreciably to other cell types or to other lymphocyte transport systems tested. 19 references.
IT **18181-93-6**
RL: BIOL (Biological study)
(amethopterin absorption by lymphocytes in response to)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

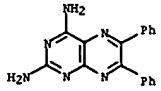


L8 ANSWER 15 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:452104 CAPLUS
DOCUMENT NUMBER: 69:52104
TITLE: Pteridines. XII. Structure-activity relation of some pteridine diuretics
AUTHOR(S): Weinstock, Joseph; Wilson, James W.; Wiebelhaus, Virgil D.; Haass, Alfred R.; Brennan, Francis T.; Sosnowski, Genevieve
CORPORATE SOURCE: Res. and Develop. Div., Smith Kline and French Lab., Philadelphia, PA, USA
SOURCE: Journal of Medicinal Chemistry (1968), 11(3), 573-9
CODEN: JMCHAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The diuretic activity of pteridines related to 2,4,7-triamino-6-phenylpteridine (triamterene), 2,4-diamino-6,7-dimethylpteridine (I), and 4,7-diamino-2-phenyl-pteridine-6-carboxamide was studied in the saline-loaded and sodium-deficient rat. A limited number of related pyrimidopyrimidines were similarly studied. Some of the compds. related to triamterene and I not only cause Na+ excretion but also conserve K+. All the 2-phenylpteridines that were studied which are active natriuretic agents also cause K+ excretion. In the triamterene series, replacement of any of the amino groups by either a large amine or a nonbasic group other than H leads to reduction of diuretic activity. Replacement of the Ph by a small, nonbasic group gives active diuretic agents, but an aromatic (or heteroaromatic) group seems desirable for highest activity. Some variation in the substitution pattern on the pteridine ring is permissible as demonstrated by the activity of the triamterene isomers. The 7-Ph isomer is outstanding as a blocker of K+ excretion.
IT **18181-93-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(as diuretic)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 16 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:118339 CAPLUS
DOCUMENT NUMBER: 54:118339
ORIGINAL REFERENCE NO.: 54:22664f-i,22665a-b
TITLE: Pteridines. XXI. One-step synthesis of 4-aminopteridines
AUTHOR(S): Taylor, Edward C., Jr.; Cheng, C. C.
CORPORATE SOURCE: Princeton Univ., Princeton, NJ
SOURCE: Journal of Organic Chemistry (1959), 24, 997-9
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 54:118339
GI For diagram(s), see printed CA Issue.
AB cf. CA 54, 5675a. The title compds., N: CR.N:C(NH2).C:C.N:CR'.CR':N(I), were prepared by heating amidine salts of (NC)2C:NOH (II) in HOCH2CH2OH, diluting the isomerized pyrimidine solution with H2O, adding Na2S2O4.2H2O (III), and finally treating with an α-diketone. II K salt (1.0 g.) and 1.1 g. guanidine carbonate (IV) in 10 ml. HOCH2CH2OH warmed gently 3 min. and the deep red solution diluted with 10 ml. H2O, 0.6 g. III added and the mixture heated 20 min. on a steam bath, the clear yellow solution acidified to pH 6 with HCl and warmed 15 min. on a steam bath with 1 ml. Ac2, diluted with 20 ml. alc., and the chilled solution filtered yielded 75% authentic I (R = NH2, R' = Me) (V). II K salt (1.5 g.), 1.5 g. IV, and 12 ml. HOCH2CH2OH heated 3 min. and reduced with 1.0 g. III, the alkaline solution refluxed 1 hr. with 10 ml. EtCOMe in 5 ml. alc., and the filtered solution chilled yielded 29% I (R = NH2, R' = Ph) (VI). II K salt (3 g.) and 3.3 g. IV in 20 ml. hot HOCH2CH2OH reduced with 1.0 g. III and the pale yellow solution adjusted to pH 3 with HCl, stirred 40 min. at 110° with 7.5 g. glyoxal bisulfite in 50 ml. H2O and the mixture kept overnight at room temperature, acidified with AcOH, and the separated product (3.55 g.) sublimed at 240°/0.05 mm. gave authentic I (R = NH2, R' = H) (VII). II K salt (2.0 g.) and 2.2 g. IV isomerized and reduced, the solution diluted with 20 ml. N HCl and treated with 2.0 g. alloxan, the purple mixture shaken with gradual separation of an orange solid and adjusted to pH 9 with KOH, the alkaline solution heated 10 min. at 110° and reacidified to pH 6 with HCl, refrigerated, and filtered gave 76% orange 2,4-diamino-5,7-dihydroxypyrimido[5,4-g]pteridine (VIII), m. above 350°. II benzamidine salt (2.0 g.) and 10 ml. 2-picoline heated 30 min. at 135° and the mixture diluted with 20 ml. H2O, the blue-green suspension evaporated in vacuo and the residue heated to 90-100° in 25 ml. H2O, treated portionwise with 1.6 g. III and the yellow solution stirred 20 min., refluxed 2 hrs. with 2 g. Bz2 in 30 ml. 1:1 EtCOMe-alc., and the cooled mixture filtered gave 1.9 g. 4-amino-2,6,7-triphenylpteridine (IX), m. 255°, λ 290, 377 mμ (log ε 4.53, 4.23, alc.). Paper chromatographic analysis in a series of systems by the descending method at 22° gave fluorescent spots (pteridine, Rf with 4% Na citrate, 3% NH4Cl, 2:1 5N BuOH-AcOH, and 2:1 PrOH-1% NH4OH given): V, 0.25, 0.54, 0.43, 0.65; VI, 0.08, 0.17, 0.73, 0.88; VII, 0.27, 0.54, 0.28, 0.51; VIII, 0.23, 0, 0, 0; IX, 0, -, 0.88, 1. Except as indicated, I

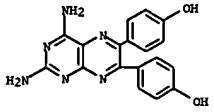
L8 ANSWER 16 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
prepd. by this one-step method were chromatographically pure.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- (preparation of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



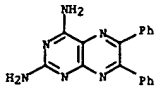
L8 ANSWER 17 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1959:40178 CAPLUS
DOCUMENT NUMBER: 53:40178
ORIGINAL REFERENCE NO.: 53:7261i,7262a-b
TITLE: Effect of 4-amino folic antagonists on biological acetylations
AUTHOR(S): Johnson, Willard J.; Corte, George; Jasmin, Roland
CORPORATE SOURCE: F. W. Horner Labs., Montreal, Can.
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1958), 99, 677-80
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 50, 15662f. Acetylation of sulfanilamide and of isoniazid in pigeon-liver exts. was markedly inhibited (noncompetitively) by 4-amino analogs of folic acid. Amethopterin (10-5M) and aminopterin (5 + 10-5M) inhibited acetylation about 60%. Folic acid (10-3M) was not inhibitory, and failed to reverse the inhibition by Amethopterin. 2,4-Diamino-6,7-diphenylpteridine (10-3M) gave 5% inhibition and 2,4-diaminopteridine (10-3M) was inactive. Amethopterin, administered to rabbits cojointly with sulfanilamide, resulted in a marked increase in plasma level of free sulfanilamide with concomitant decrease in acetylsulfanilamide. The possible significance of these results with regard to combination chemotherapy of cancer is discussed.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- (acetylation inhibition in liver by)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

L8 ANSWER 18 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1956:52652 CAPLUS
DOCUMENT NUMBER: 50:52652
ORIGINAL REFERENCE NO.: 50:10103e-g
TITLE: Route to 4-aminopteridines
AUTHOR(S): Taylor, E. C., Jr.; Paudler, W. W.
CORPORATE SOURCE: Princeton Univ., Princeton, NJ
SOURCE: Chemistry & Industry (London, United Kingdom) (1955) 1061-2
CODEN: CHINAG; ISSN: 0009-3068
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 50:52652
AB A new route for 4-amino-5,6-diphenylpteridines (I) is described. 2-Hydroxy-5,6-diphenylpyrazinamide (II) (Jones, C.A. 43, 3009h) gave 99% yield 2-chloro-3-cyano-5,6-diphenylpyrazine (III) when heated in a sealed tube with PCl3. III was also obtained in 80% yield by heating a mixture of II, POCl3, and PCl5. Fusion of III with guanidine carbonate, urea, or thiourea gave 65, 59, and 51% 2-amino, 2-hydroxy, and 2-mercapto derivs. of I, resp. III with N2H4.H2O gave 2-chloro-5,6-diphenylpyrazinoic acid hydrazide, or when repeated in the presence of KI gave 3-amino-5,6-diphenyl-1-pyrazolo[b]pyrazine. III gave 2-amino-5,6-diphenylpyrazinamide when treated with NH4OH and KI, or 2-amino-3-cyano-5,6-diphenylpyrazine when fused with NH4OAc.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- (preparation of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

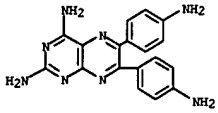
L8 ANSWER 22 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN Phenol, 4,4'-(2,4-diamino-6,7-pteridinediyl)bis- (9CI) (CA INDEX NAME)



RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

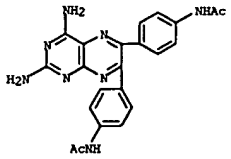


RN 151648-52-1 CAPLUS
CN 2,4-Pteridinediamine, 6,7-bis(4-aminophenyl)- (9CI) (CA INDEX NAME)

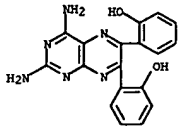


RN 804555-05-3 CAPLUS
CN Acetanilide, 4'-[7-(p-acetamidophenyl)-2,4-diamino-6-pteridyl]- (5CI) (CA INDEX NAME)

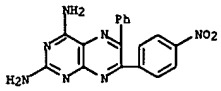
L8 ANSWER 22 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



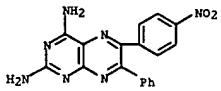
RN 855404-13-6 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



RN 857397-78-5 CAPLUS
CN Pteridine, 2,4-diamino-7-(p-nitrophenyl)-6-phenyl- (5CI) (CA INDEX NAME)

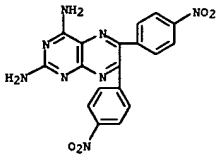


RN 857397-80-9 CAPLUS
CN Pteridine, 2,4-diamino-6-(p-nitrophenyl)-7-phenyl- (5CI) (CA INDEX NAME)

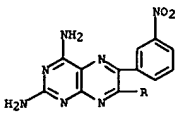


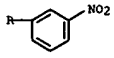
RN 857398-09-5 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis[p-nitrophenyl]- (5CI) (CA INDEX NAME)

L8 ANSWER 22 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 857398-11-9 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis[m-nitrophenyl]- (5CI) (CA INDEX NAME)





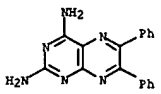
L8 ANSWER 23 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1955:17275 CAPLUS
DOCUMENT NUMBER:	49:17275
ORIGINAL REFERENCE NO.:	49:3417g-i
TITLE:	Some 2,4-diaminopteridines as folinic acid antagonists
AUTHOR(S):	Collier, H. O. J.; Phillips, Margaret
CORPORATE SOURCE:	Allen & Hanburys, Ltd., Ware, UK
SOURCE:	Nature (London, United Kingdom) (1954), 174, 180-1 CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE:	Journal
LANGUAGE:	Unavailable

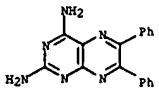
AB The antifolinic acid activity of amethopterin (I) may be related to its antileukemia action. Some 2,4-diaminopteridines (II), known to be antagonistic to pteroylglutamic acid, were tested for antileukemia activity. Inhibition of acid production of Leuconostoc citrovorum was the measure used. Potency of II as folinic acid antagonists depended on the 6,7-substituents of the pteridine ring. In the 6,7-dialkyl series, peak activity was obtained with 6,7-di-sec-butyl-(III) and 6,7-diisopropyl-2,4-diaminopteridine (IV). In the 6,7-indolo series, peak activity was obtained with 6,7-[N-propylindolo(2',3')]-2,4-diaminopteridine. Activity was slight in the 6,7-(CH3)2 and 6,7-(Ph)2 compds. and the unsubstituted compound was inactive. Omission of one amino group in II reduced activity. Members of I were antimalarial, but this activity could not be correlated with antifolinic activity. The inhibition factors of I, II, and III at 5 mg./mL. levels of folinic acid were very close.

IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl-
(as folinic acid antagonist)

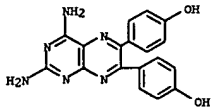
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



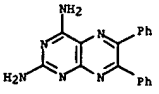
L8 ANSWER 19 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1955:84700 CAPLUS
DOCUMENT NUMBER: 49:84700
ORIGINAL REFERENCE NO.: 49:16014i,16015a-b
TITLE: Synthesis of compounds related to thymine. II. Effect of thymine antagonists on the biosynthesis of DNA (deoxyribonucleic acid)
AUTHOR(S): Bardos, Thomas J.; Levin, Georgia M.; Herr, Ross R.; Gordon, Harry L.
CORPORATE SOURCE: Armour Labs., Chicago
SOURCE: Journal of the American Chemical Society (1955), 77, 4279-86
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. ibid. 960-3. The patterns of DNA biosynthesis were studied in Lactobacillus leichmannii and L. plantarum. The modes of action of various metabolic antagonists, particularly 5-bromouracil and its nucleosides, are discussed. The systems described are used to study the biol. action of 3 new thymine antagonists: 5-mercaptouracil, 5-uracilyl disulfide, and uracil-5-isothiouronium chloride. Deoxyuridine (2.28 g.) in 50 cc. water treated with saturated Br water, the solution aerated, lyophilized, the residue in 250 cc. absolute EtOH refluxed 15 min., and concentrated in vacuo to 30 cc. yielded 0.82 g. 5-bromodeoxyuridine, m. 181-3°.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- (effect on deoxyribonucleic acid formation in Lactobacillus)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 20 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1955:44060 CAPLUS
DOCUMENT NUMBER: 49:44060
ORIGINAL REFERENCE NO.: 49:8484a-c
TITLE: Phenolic compounds as chemotherapeutic agents against poliomyelitis virus in tissue culture
AUTHOR(S): Kramer, Patricia Elly; Robbins, Mary Louise; Smith, Paul K.
CORPORATE SOURCE: George Washington Univ., Washington, DC, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1955), 113, 262-71
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Tests were made on 135 phenolic compds. and 20 nonphenolic benzene derivs. Only 19 compds. were found to inhibit proliferation of type 2 poliomyelitis virus, Y-SK strain, in roller cultures of monkey testicular tissue inoculated at the same time with drug and virus. Fifteen (all diphenols or aminophenols) were capable of inhibiting virus-induced degeneration of the fibroblasts over a wide range of concentration, independent of whether the virus was inoculated 24 h. before or after treatment with the drug. Twenty-six compds. naturally occurring in tissues were tested for ability to reverse the inhibitory action of the drugs. Glutathione reversed the action of 12. Serine, threonine, and hydroxyproline frequently inhibited the action of one or more of the drugs.
IT 6967-77-7, Pteridine, 2,4-diamino-6,7-bis(p-hydroxyphenyl)- (effect on poliomyelitis virus in tissue culture)
RN 6967-77-7 CAPLUS
CN Phenol, 4,4'-(2,4-diamino-6,7-pteridinediyl)bis- (9CI) (CA INDEX NAME)



L8 ANSWER 21 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1955:29379 CAPLUS
DOCUMENT NUMBER: 49:29379
ORIGINAL REFERENCE NO.: 49:5678i,5679a-b
TITLE: Action of 2,4-diamino-6,7-diisopropylpteridine upon Plasmodium gallinaceum and its relation to other compounds which are pteroylglutamic acid antagonists
AUTHOR(S): Bishop, Ann
CORPORATE SOURCE: Univ. Cambridge, UK
SOURCE: Parasitology (1954), 44, 450-64
CODEN: PARAAE; ISSN: 0031-1820
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Two strains of P. gallinaceum were made resistant to 2,4-diamino-6,7-diisopropylpteridine (I) by passing the parasite through chicks which had been treated with the drug. Passages at 2-4-day intervals maintained a state of acute infection, and large nos. of the parasites were exposed to the drug. Dosages were kept slightly below the maximum tolerated by the parasite. Strains resistant to I were resistant to proguanil (II), pyrimethamine (III), 2,4-diamino-6,7-diphenylpteridine (IV), 2,4-diamino-5-(p-chlorophenoxy)-6-methylpyrimidine, but not to sulfadiazine (V). In one strain, development of resistance to I was developed at a faster rate than resistance to II, and resistance to II was obtained faster than resistance to III. A strain made resistant to IV was resistant to I, II, and III, but not to V. The action of I and II was not antagonized by p-aminobenzoic acid, though in the min. effective dose their action was antagonized by relatively large doses of pteroylglutamic acid. The action of V was antagonized competitively by p-aminobenzoic acid but only by pteroylglutamic acid when the V was given in small doses.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- (effect on Plasmodium gallinaceum)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 22 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1955:20270 CAPLUS
DOCUMENT NUMBER: 49:20270
ORIGINAL REFERENCE NO.: 49:4030f-i,4031a
TITLE: 2,4-Diaminopteridine and derivatives
INVENTOR(S): Cain, Cornelius K.
PATENT ASSIGNEE(S): Research Corp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2667486		19540126	US 1951-228139	19510524

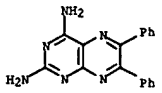
AB A new series of antibacterial compds., 2,4-diaminopteridine, also called 2,4-diaminopyrimido[4,5-b]pyrazine, and its substitution products, are prepared from 2,4,5,6-tetraaminopyrimidine (I) or its salts with 1,2-dicarbonyl compds., 1,2-dicarboxylic acids, or with α-carbonyl acids or their derivatives such as esters, etc., in aqueous, nonaq., or mixed solns. of acidic, neutral, or basic reaction. On the pyrimidine ring are located 2 amino groups, at the 2- and the 4-position, making this new synthetic pterin to be the first to have a 2,4-diamino structure, unlike folic acid. Thus, 2,4-diaminopteridine was prepared by adding 2 g. I sulfate in 70 cc. hot H2O, to 3.5 g. of glyoxal bisulfite in 30 cc. of hot water, boiling the clear yellow mixture 15 min., treating with C, allowing to cool slowly, filtering off the light yellow microcryst. precipitate, washing with water and Me2CO, drying in vacuo, and purifying by recrystn. from H2O or by sublimation at 180°/1 mm. Other compds. prepared are 2,4-diamino-7-methylpteridine; 2,4-diamino-7-pteridinecarboxylic acid, light yellow microcryst. solid darkening slowly without melting on heating to 300°; 2,4-diamino-6,7-bis(p-aminophenyl)pteridine; 2,4-diaminophenanthro[9,10-e]pyrimido[4,5-b]pyrazine-8- (or 11)sulfonic acid; 2,4-diamino-6,7-dihydroxypteridine; 2,4-diamino-6,8-dihydroxydipyrimido[4,5-b,5',4'-e]pyrazine; 2,4-diamino-6,7-dimethylpyrimido[4,5-b]pyrazine; 2,4-diamino-6,7-diphenylpyrimido[4,5-b]pyrazine; 2,4-diaminoacenaphtho[1,2-e]pyrimido[4,5-b]pyrazine; 2,4-diaminophenanthro[9,10-e]pyrimido[4,5-b]pyrazine; 2,4-diamino-6,7-bis(p-acetamidophenyl)pteridine; 2,4-diamino-6,7-bis-(m-nitrophenyl)pteridine. Other typical compds. which may be made by the methods heretofore described are the following derivs. of 2,4-diaminopteridine; 7-Ph, m. 338-340°; 6-Me, m. 314-320°; 6-HO, decompose above 300°; 6,7-(p-HOC6H4)2, decompose above 300°; 6,7-(m-O2NC6H4)2, m. 307-8°; 6-(p-O2NC6H4), m. 314-15°; 6,7-(HOC6H4)2, m. 304-6°; 6,7-(p-O2NC6H4)2, m. 343°; 6-Ph, 7-(p-O2NC6H4), m. 307-8°.
IT 6967-77-7, Pteridine, 2,4-diamino-6,7-bis[p-hydroxyphenyl]- 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- 151648-52-1, Pteridine, 2,4-diamino-6,7-bis(p-aminophenyl)- 804555-05-3, Acetanilide, 4'-[7-(p-acetamidophenyl)-2,4-diamino-6-pteridyl]- 855404-13-6, Pteridine, 2,4-diamino-6,7-bis[o-hydroxyphenyl]- 857397-78-5, Pteridine, 2,4-diamino-7-(p-nitrophenyl)-6-phenyl- 857397-80-9, Pteridine, 2,4-diamino-6-(p-nitrophenyl)-7-phenyl- 857398-09-5, Pteridine, 2,4-diamino-6,7-bis[p-nitrophenyl]- 857398-11-9, Pteridine, 2,4-diamino-6,7-bis[m-nitrophenyl]- (preparation of)
RN 6967-77-7 CAPLUS

L8 ANSWER 24 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1954:3619 CAPLUS
DOCUMENT NUMBER: 48:3619
ORIGINAL REFERENCE NO.: 48:689a-g
TITLE: Pteridines. VII. The synthesis of 2-alkylaminopteridines
AUTHOR(S): Taylor, E. C., Jr.; Caine, C. K.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Journal of the American Chemical Society (1952), 74, 1644-7
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C.A. 47, 137h. The synthesis of several 4-amino-2-alkylaminopteridines is described. The ultraviolet absorption spectra are reported, and the effects of alkyl substitution in the 2-NH2 group of a 2,4-diaminopteridine on the spectra and phys. properties of the compound are given. Replacement of the H atoms of the 2-NH2 group of 2,4-diamino-6,7-diphenylpteridine (I) by alkyl groups reduces the antifolic activity. 4,6-Diamino-2-mercaptopyrimidine (30 g.), 36 g. MeI, and 150 cc. absolute EtOH refluxed 1 hr., the solution filtered with C, the filtrate evaporated to dryness in vacuo, the residue in 100 cc. hot water adjusted to pH 9 with NH4OH, the solid in 200 cc. Me2CO heated to boiling, filtered, the Me2CO removed in vacuo, and the residue dissolved in 200 cc. boiling water and cooled rapidly yielded 27.5 g. 4,6-diamino-2-methylmercaptopyrimidine (II), m. 188-9°. The 5-nitroso derivative of II (10 g.) in 180 cc. boiling water treated portionwise with 27.1 g. Na dithionite, the solution filtered with C, the filtrate treated with 50 cc. 50% H2SO4 and cooled to 0° yielded 9.98 g. 4,5,6-triamino-2-methylmercaptopyrimidine sulfate (III). 4,5,6-Triamino-2-mercaptopyrimidine sulfate (IIIA) (1.0 g.) in 125 cc. boiling water adjusted to pH 7 with dilute NaOH, the solution treated with 0.5 g. Ac2 in 5 cc. EtOH and the mixture cooled to 0° yielded 0.755 g. 4-amino-2-mercapto-6,7-dimethylpteridine (IV), decompose above 280°. III yielded 59% 4-amino-2-methylmercapto-6,7-dimethylpteridine (V), m. 274-5°. IIIA (1.0 g.) in 25 cc. boiling water adjusted to pH 9 treated with 0.95 g. benzil in 10 cc. each EtOH and EtCOMe, the mixture refluxed 3 hrs., the organic solvents removed in vacuo, and the aqueous residue acidified with AcOH yielded 1.09 g. 4-amino-2-mercapto-6,7-diphenylpteridine (VI), m. 283°. III and benzil yielded 47% 4-amino-2-methylmercapto-6,7-diphenylpteridine (VII), m. 252.5-53°. VI (0.15 g.) in 50 cc. absolute EtOH and 0.10 g. MeI refluxed 30 min., the solution evaporated nearly to dryness in vacuo, the residue in 40 cc. 0.1N NH4OH evaporated to dryness, the residue in 50 cc. boiling EtOH treated with C and the filtrate diluted with 50 cc. water yielded 0.110 g. VII, m. 252.5-53°. Approx. 0.20 g. pteridine, 1.0 g. amine, and 50 cc. absolute EtOH heated 10 hrs. at 180° yielded the following alkylpteridines (pteridine, amine, product, % yield, and m.p. given): IV, NH3, I, 84, 280-3° (uncor.); V, NH3, I, 79, -; VI, MeNH2, 4-amino-2-methylamino-6,7-diphenylpteridine (VIII), 97, 264-5°; VII, MeNH2, VIII, 68, -; VI, Me2NH, 4-amino-2-dimethylamino-6,7-diphenylpteridine (IX), 97, 192-5°; VII, Me2NH, IX, 94, -; IV, Me2NH, 4-amino-2-dimethylamino-6,7-dimethylpteridine (X), 93, decompose above 260°; V, Me2NH, X, 53, -. VI (1.0 g.), 15 cc. piperidine,

L8 ANSWER 24 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
and 10 cc. HCONMe2 refluxed 12 hrs., the soln. distd. in vacuo, the residue poured into 100 cc. water, and the oil in a few cc. Me2CO poured into 50 cc. ice water yielded 0.75 g. 4-amino-2-piperidino-6,7-diphenylpteridine m. 209°. VI (0.70 g.) and 10 cc. morpholine refluxed 10 hrs., the mixt. dild. with water, let stand overnight at 2°, filtered, the product in Me2CO treated with C and the filtrate evapd. to dryness yielded 0.37 g. the 2-morpholino analog, m. 231-2°.

IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- (alkyl derivs.)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



(prepn. of

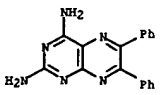
L8 ANSWER 25 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1952:60851 CAPLUS
DOCUMENT NUMBER: 46:60851
ORIGINAL REFERENCE NO.: 46:10212d-g
TITLE: Improvements in the preparation of sulfonyl derivatives of piperazine
PATENT ASSIGNEE(S): Societe des usines chimiques de Rhone-Poulenc
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 661537		19511121	GB	

GI For diagram(s), see printed CA Issue.

AB Piperazine derivs. of the general formula RN(CH2.CH2)2NSO2(CH2)nSO2N(CH2.CH2)2NR (I) are prepared by treating XO2S(CH2)nSO2X (II) with a N-substituted piperazine. A II (X = Cl, n = 5) (8.5 g.) in 400 ml. Et2O is added drop by drop over a period of 0.5 hrs. with agitation to 12.35 g. MeN(CH2.CH2)2NH in 40 ml. ice-cooled anhydrous Et2O, agitation is continued 3 hrs. at room temperature, the precipitate centrifuged and washed with Et2O; the I (n = 5, R = Me) so obtained, purified by extraction with Et2O in a Soxhlet apparatus and recrystn. from EtOAc, m. 102-3°. The following compds. I were prepared in a similar manner (n, R, and m.p. given): 3, Et, 97-98°; 4, Et, 171°; 5, Et, 110-11°; 6, Et, 147°. The disulfonyl halides (II) may be prepared by treating Br(CH2)nBr with NH2CSNH2, which gives the thiocarbamido derivative, (HBr.NH:)NH2CS(CH2)nCSC(NH2):NH.HBr (III). This latter product with KOAc gives the corresponding diacetate (IV). II is formed by treating IV in water with a halogen. The III so prepared are (n and m.p. given): 5, 170°; 3, 205°; 4, 215°; 6, 205°. IV: 3, 194-6°; 4, 209-11°; 6, 168-70°, II: 5, 64°; 3, 46°; 4, 82-4°; 6, 86°. These compds. are effective in the treatment of states of traumatic or hemorrhagic shock.

IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- (preparation of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

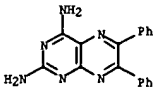


L8 ANSWER 26 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1952:60850 CAPLUS
DOCUMENT NUMBER: 46:60850
ORIGINAL REFERENCE NO.: 46:10212d
TITLE: Pyrimidopyrazines
INVENTOR(S): Timmis, Geoffrey M.
PATENT ASSIGNEE(S): Wellcome Foundation Ltd.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 674847		19520702	GB	

AB See U.S. 2,581,889 (C.A. 46, 7594g).

IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- (preparation of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

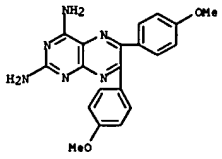


L8 ANSWER 27 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1952:57451 CAPLUS
DOCUMENT NUMBER: 46:57451
ORIGINAL REFERENCE NO.: 46:9623d-i
TITLE: 6- and 7-Bromomethyl pteridines
INVENTOR(S): Boothe, James H.
PATENT ASSIGNEE(S): American Cyanamid Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2584538		19520205	US 1948-35069	19480624

AB Compds. useful as intermediates in the preparation of pteroylglutamic acid (I) and related compds. are prepared as 2-Amino-4-hydroxy-6-methylpteridine (II) 12 g., 48% HBr 400, and Br 12 cc. are heated overnight on a steam bath, the mixture chilled overnight, and the crystals isolated mechanically and crystallized from 48% HBr by a current of air-Br, and then from hot AcOH containing 1-5% HBr, to give 2-amino-4-hydroxy-6-(dibromomethyl)pteridine-HBr (III). II 50 g., Br 50, and 48% HBr 1500 cc. are heated 20 hrs. on a steam bath, and the solution concentrated to 500 cc., chilled at -5° overnight, filtered, concentrated to 350 cc., and cooled to give 38 g. III. The final filtrate is evaporated to dryness, and the residue suspended in 1 l. H2O, shaken, collected, and washed with H2O, alc., and Et2O to give 6-(bromomethyl)pteridine, which with N-(p-aminobenzoyl)glutamic acid gives 9-27% I. II 20 g., 48% HBr 1 l., and Br 12 cc. are refluxed 1 hr., the solution concentrated to 500 cc., treated with 21 g. C, filtered, added to 3.5 l. cold H2O, and neutralized to pH 3-5 with NaOAc to give 24 g. III (free base). Br 50 g. in 48% HBr 300 cc. is added dropwise with stirring to 2-amino-4-hydroxy-7-methylpteridine (IV) 50 g. in 48% HBr 3 l., and the mixture heated 20 min. to give 2-amino-4-hydroxy-7-(bromomethyl)-pteridine. Br 40 cc. is added to IV 40 g. in 48% HBr 1200 cc. at 70-95°, and the solution heated 2 hrs. on the steam bath to give 47.7 g. 2-amino-4-hydroxy-7-(dibromomethyl)pteridine (V). IV 2 g., 48% HBr 40 cc., and Br 4 g. are heated 45 min. just under reflux temperature, the solution freed of excess Br, cooled, and the precipitate suspended in H2O containing several drops of pyridine to give 2.3 g. V. Br 1.34 cc. in 48% HBr 10 cc. added to 2-amino-4-hydroxy-6,7-dimethylpteridine 5 g. at 95° gives 3.5 g. 2-amino-4-hydroxy-6-methyl-7-(bromomethyl)-pteridine. (BrCH2CO)2 1.22 g. in alc. 10 cc. added to 2,4,5-triamino-6-hydroxypyrimidine-2HCl in 2.5 N HBr 25 cc. gives 0.9 g. of a substance of the same composition as 6,7-dibromodimethylpterin (VI). H2O is added to VI 15 g. in 48% HBr 210 cc. to give 750 cc. of solution; KI 7.13 g. in H2O 25 cc. is added during 1 hr. at 55° and the solution held 1 hr. at 55°, cooled to 15°, treated with NaHSO3 until the dark color is discharged, filtered, and neutralized to pH 1 with saturated NaOAc solution to give 12.1 g. 2-amino-4-hydroxy-6-bromomethyl-7-methylpteridine. Br 250 mg. is added to 2-amino-4-hydroxy-6-methylpteridine 200 mg. in (HOCH2)2 7.5 cc. and 48% HBr 0.5 cc. at 50°, the soln. heated 45 min. at 50-70°, mixed with (HOCH2)2 7.5 cc. contg. N-(p-aminobenzoyl)glutamic acid 0.5 g., buffered at pH 4 with 1 g. KOAc, and heated overnight at 100° to give 0.2 g. of material contg. 8.29% I. Cf. C.A. 46, 3092d.

IT 694514-86-8, Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)-
(preparation of)
RN 694514-86-8 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)- (5CI) (CA INDEX NAME)

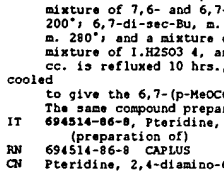


L8 ANSWER 28 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1952:57450 CAPLUS
DOCUMENT NUMBER: 46:57450
ORIGINAL REFERENCE NO.: 46:9623b-d
TITLE: Substituted pteridines
INVENTOR(S): Campbell, Norman R.; Fitzgerald, Maurice E. H.; Collier, Henry O. J.
PATENT ASSIGNEE(S): Allen & Hanburys Ltd.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 656769		19510829	GB	

AB Compds. which have antibacterial properties, especially against Vibrio cholerae, are prepared as follows. A mixture of (EtCO)2 1,2,4,5,6-tetraaminopyrimidine acetate (I) 1 mol., and 60% AcOH 2.5 l. are refluxed 2 hrs., cooled, poured into 20 l. H2O, and adjusted to pH 6 to give 6,7-diethyl-2,4-diaminopteridine (II), m. 280° (from EtOH). Similarly prepared are the following analogs of II: 6,7-di-iso-Pr, m. 246°; a mixture of 7,6- and 6,7-Et(p-MeOC6H4), m. 228°; a mixture of 7,6- and 6,7-iso-Pr(p-MeOC6H4), m. 200°; 6,7-di-Pr, m. 200°; 6,7-di-sec-Bu, m. 210°; a mixture of 7,6- and 6,7-EtPh, m. 280°; and a mixture of 7,6- and 6,7-isoPrPh, m. 242°. A mixture of I.H2SO3 4, anisil 5 g., MeCOEt 40, H2O 80, EtOH 40, and HCl 2.4 cc. is refluxed 10 hrs., filtered, neutralized with NaOH solution, and cooled to give the 6,7-(p-MeOC6H4)2 analog of II, m. 281° (from pyridine). The same compound prepared similarly to II m. 288°.

IT 694514-86-8, Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)-
(preparation of)
RN 694514-86-8 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)- (5CI) (CA INDEX NAME)

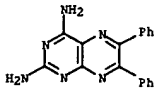


L8 ANSWER 29 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1952:45488 CAPLUS
DOCUMENT NUMBER: 46:45488
ORIGINAL REFERENCE NO.: 46:7594g-i,7595a
TITLE: Pyrimidopyrazines
INVENTOR(S): Timmis, Geoffrey M.
PATENT ASSIGNEE(S): Burroughs Wellcome and Co. (U.S.A.) Inc.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

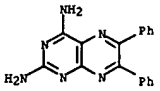
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2581889		19520108	US 1949-103319	19490706

AB Nitrosoaminopyrimidines in acidic media with a ketone containing an activated -CH2- group yield pyrimidopyrazines whose structures are unequivocally known. E.g., 2 g. 5-nitroso-2,4,6-triaminopyrimidine, 4 g. PhCH2COPh (I), 60 cc. glacial HOAc, and 1 drop concentrated HCl are heated 9 hrs. at 150-60°, cooled, the yellow solid filtered, the filtrate diluted with 250 cc. H2O and 20 cc. 2 N HCl, shaken twice with 50 cc. Et2O, then with 50 cc. light petr. ether to remove unchanged I, the solution made alkaline with concentrated NH4OH, and the precipitate filtered, washed with H2O and MeOH, and dried, yielding 1.1 g. 2,4-diamino-6,7-diphenylpyrimido-[4,5-b] pyrazine (C.A. numbering throughout), m. 282° (from 50% HCO2H). Similarly prepared are 2,4-diamino-6H-indolo[2,3-g]pteridine, does not m. under 350°; 2,4-diaminopyrimido[4,5-b]quinoxaline; 2,4-diamino-6-phenyl-7-methylpyrimido[4,5-b]pyrazine, m. 332°; 2,4-diamino-6-methyl-7-phenylpyrimido[4,5-b]pyrazine, m. 332°; 6,8-di-aminodipyrimido[4,5-b,5',4'-e]pyrazine-2,4-diol; dipyrimido-[4,5-b,5',4'-e] pyrazine-2,4,6,8-tetrol, does not m. below 350°; 8-aminodipyrimido [4,5-b, 5', 4'-e] pyrazine-2,4, 6-triol, does not m. below 350°; 1,3,7,9-tetramethyldipyrimido[4,5-b,5',4'-e]-pyrazine-2,4,6,8(1H,3H,7H,9H)-tetrone, m. 403°. These compds. are useful therapeutic agents.

IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl-
(preparation of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

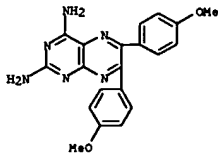


L8 ANSWER 30 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1952:36322 CAPLUS
DOCUMENT NUMBER: 46:36322
ORIGINAL REFERENCE NO.: 46:6197a-d
TITLE: The activities of some 2,4-diaminopteridines and sulfathiazole against Streptococcus faecalis and Staphylococcus aureus
AUTHOR(S): Collier, H. O. J.; Waterhouse, Pamela D.
CORPORATE SOURCE: Allen & Hanburys Ltd., Ware, UK
SOURCE: British Journal of Pharmacology and Chemotherapy (1952), 7, 161-9
CODEN: BJPCAL; ISSN: 0366-0826
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 45, 5815i. In vitro tests were made with 6,7-disubstituted 2,4-diaminopteridines as growth inhibitors against 4 strains of S. faecalis. The greatest activity was shown by dialkyl derivs. with straight or branched chains containing 3-6 C, the dibenzyl (I) derivative, and 1'-methyl-indolo-(2',3',6,7)-2,4-diaminopteridine. Highest activity was shown against strains requiring preformed pteroylglutamic acid (II). Sulfathiazole (III) potentiated the inhibitory effect of I against strains of S. faecalis not requiring II. The presence of 5% urine or oxalated horse blood did not appreciably antagonize the inhibitory effect of I. Against S. aureus, I, bis(cyclohexylmethyl), and normal dialkyl compds. were most active. In the dialkyl series peak activity occurred in the dibutyl and diamyl derivs. The toxicity of I was similar to that of III. I phosphate prolonged the lives of mice infected with S. aureus. It also acted synergistically with III both in vitro and in vivo in protecting mice against infections of S. aureus.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl-
694514-86-8, Pteridine, 2,4-diamino-6,7-bis[p-methoxyphenyl]-
857228-94-5, Pteridine, 2,4-diamino-6,7-bis[o-methoxyphenyl]-
(antibacterial action of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

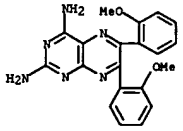


RN 694514-86-8 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)- (5CI) (CA INDEX NAME)

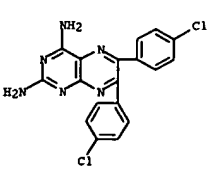
L8 ANSWER 30 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 857228-94-5 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis[o-methoxyphenyl]- (5CI) (CA INDEX NAME)

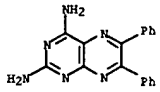


L8 ANSWER 31 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1952:27482 CAPLUS
DOCUMENT NUMBER: 46:27482
ORIGINAL REFERENCE NO.: 46:4675b-e
TITLE: 2, 4-Diaminopyrimidines. A new series of antimalarials
AUTHOR(S): Falco, E. A.; Goodwin, L. G.; Hitchings, G. H.; Rollo, I. M.; Russell, P. B.
CORPORATE SOURCE: Wellcome Research Labs., Tuckahoe, NY
SOURCE: British Journal of Pharmacology and Chemotherapy (1951), 6, 185-200
CODEN: BJPCAL; ISSN: 0366-0826
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. Nature 164, 1133(1949). Many members of a series of 158 derivs. of 2,4-diaminopyrimidine which were prepared and tested showed high antimalarial activity against infections of Plasmodium gallinaceum in chicks and Plasmodium berghei in mice. Compds. with a 5-Ph substituent were most active; 5-PhCH2 and 5-PhO derivs. were somewhat less active. Substitution of a p-NO2 or p-halogen in the 5-substituent enhanced the activity. Substitution of an alkyl group in the 6-position enhanced the activity and in the 5-Ph derivs. maximum activity was reached with the 6-Et compound 2,4-Diamino-5-(p-chlorophenyl)-6-ethylpyrimidine was 60 times as active as paludrine against P. gallinaceum and 200 times as active against P. berghei. Longer-chain alkyl derivs. were less active. The drugs were active against the blood forms of Plasmodium cynomolgi in monkeys, but had no pronounced action on the exoerythrocytic forms. Acute oral LD50 (mg./kg.) in mice, and the paludrine equivs. against P. gallinaceum and P. berghei were, in order, for the following more active 2, 4-diaminopyrimidines: 5-(p-chlorophenoxy)-6-methyl, .apprx.1000, 0.4, 0.7; 5-(p-chlorobenzyl)-6-methyl, 79, 0.4, 2.0; 5-(p-chlorophenyl), 250, 0.4, 30; 5-(p-nitrobenzyl)-6-methyl, 146, 1.0, 1.5; 5-(p-chlorophenyl)6-ethyl, 92, 60, 200; and 5-(3, 4-dichlorophenyl)-6-ethyl, 66, 20, 190, while quinine gave 1160, 0.08, 0.16, and paludrine acetate 59, 1.0, 1.0.
IT 500284-43-5, Pteridine, 2,4-diamino-6,7-bis(p-chlorophenyl)-
(antimalarial activity of)
RN 500284-43-5 CAPLUS
CN 2,4-Pteridinediamine, 6,7-bis(4-chlorophenyl)- (9CI) (CA INDEX NAME)

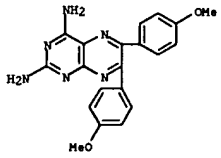


L8 ANSWER 32 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1952:17637 CAPLUS
DOCUMENT NUMBER: 46:17637
ORIGINAL REFERENCE NO.: 46:3059g-i,3060a-h
TITLE: Analogs of pteroylglutamic acid. VII. 2-Alkylamino derivatives
AUTHOR(S): Roth, Barbara; Smith, James M., Jr.; Hultquist, Martin E.
CORPORATE SOURCE: Am. Cyanamid Co., Bound Brook, NJ
SOURCE: Journal of the American Chemical Society (1951), 73, 2864-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 44, 9451e. NaOMe (22.7 g.) in 60 cc. MeOH added to 25.8 g. Me2NC(:NH)NH2 in 50 cc. dry MeOH, 20.7 g. NCCH2CO2Me added to the refluxing mixture during 10 min., and the mixture refluxed 3 hrs., filtered, and neutralized with HCl yielded 26.0 g. 2-dimethylamino-4-hydroxy-6-aminopyrimidine (I), m. 290.5-2.5° (from water). I (2 g.) in 20 cc. water warmed and acidified, the pH adjusted to 4 with NaOAc, then 0.74 g. NaNO2 in 2 cc. water added slowly at 80°, yielded the 5-nitroso derivative (II) of I, m. 259° (decomposition). Na2S2O4 (10 g.) (IIA) added at 50° to 5 g. II in 30 cc. water containing a min. of dilute NaOH yielded 3.5 g. 2-dimethylamino-4-hydroxy-5,6-diaminopyrimidine sulfite (III). III (20 g.) in 330 cc. water acidified with HCl, then warmed in vacuo, 10.7 g. N-(p-aminobenzoyl)glutamic acid (IV) added, the pH adjusted to 3.0 with NaOH, 3.98 g. Na2Cr2O7 in 23 cc. water and 17.3 g. CH2BrCHBrCHO (V) in 16 cc. AcOH added dropwise and simultaneously during 20 min. to the mixture at 45° (pH maintained at 3), and the mixture after 20 min. at 45° cooled to 10° yielded 21.3 g. assaying 24.8% N-(p-[(2-dimethylamino-4-hydroxy-6-pteridylmethyl)amino] benzoyl)-glutamic acid (VI). Purification by solution and precipitation yielded VI, assaying 85.1%. Ac2 (1 g.) and 2.9 g. III in 30 cc. water heated 45 min. at 85°, cooled, and neutralized with NH4OH yielded 2-dimethylamino-4-hydroxy-6,7-dimethylpteridine, m. 283-8° (from alc.) (decomposition). NH2C(:NH)NHCN (VIA) (50 g.) and 100 g. Me2NH.HCl heated 3 hrs. at 180°, the mixture poured into 600 cc. absolute EtOH, the solution cooled to 10°, filtered, 58.5 g. NaOMe added, then 66.7 g. CH2(CN)2 dropwise during 20 min. to the refluxing mixture, and the mixture refluxed 2 hrs., cooled, filtered, and the product washed with ice water yielded 61 g. 2-dimethylamino-4,6-diaminopyrimidine (VII), m. 259-60° (from dilute alc.). H2SO4 (5 N) added to 10 g. VII in 200 cc. water to obtain solution, the pH adjusted to about 4 with NaOAc, and 25% NaNO2 added to the solution at 85° to a permanent starch-KI test yielded 11.2 g. 2-dimethylamino-4,6-diamino-5-nitrosopyrimidine (VIII). VIII (42.9 g.) in 550 cc. water adjusted to pH 2.5 with 5 N HCl, 130 g. IIA added slowly at 60°, and the mixture heated to 70°, then acidified to approx. pH 2 with dilute H2SO4, yielded 56 g. 2-dimethylamino-4,5,6-triaminopyrimidine sulfate (IX). IX (21.3 g.) and 19.5 g. BaCl2.2H2O in 330 cc. water warmed 10 min. to 60°, cooled to 45°, then treated with IV and V as for VI yielded N-(p-[(2-dimethylamino-4-amino-6-pteridylmethyl)amino]benzoyl)glutamic acid (X). VIII (5 g.) and 4.59 g. BaCl2 in 50 cc. water heated on the steam bath 10 min., filtered hot, and 1.62 g. Ac2 added yielded 2-dimethylamino-4-amino-6,7-dimethylpteridine-HCl, bright yellow crystals from dilute alc. MeNH2.HCl (1 kg.) and 620 g. VIA heated 3 hrs. at 180°, the melt cooled to 100°, poured into 6 l. absolute EtOH, 1,440 g. NaOMe added to the filtrate, then 1,280 g. NCCH2CO2Et during 30 min., and the mixture refluxed 4 hrs. yielded 550 g.

L8 ANSWER 32 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
3-methyl-2,6-diamino-4(3H)-pyrimidone (XI), m. 265-72° (depending on the rate of heating); the cooled filtrate yielded 20 g. addnl. material; the filtrate concd. to 2 l. yielded 442 g. 2-methylamino-4-hydroxy-6-aminopyrimidine (XII), m. 227-9° (from alc. and water). 2-Methylmercapto-4-hydroxy-6-aminopyrimidine (Johns and Baumann, C.A. 7, 2388) (10 g.) and 40 cc. 25% MeNH2 heated 5 hrs. at 120° yielded a white cryst. product, m. 245-7.5°; nitroso deriv., C6H9N5O2. XII (9 g.) nitrosated yielded 9.5 g. orange ppt. (XIII) which did not m. below 360°. XIII (9 g.) reduced with 22 g. IIA yielded 2-methylamino-4-hydroxy-5,6-diaminopyrimidine sulfate (XIV), C5H9N5O.0.5H2SO4.0.5H2O. XIV (1 g.) in 100 cc. water at 60° treated with 1 g. Ac2, and the mixt. heated 15 min. at 60-70°, allowed to stand overnight, and concd. to 25 cc. yielded 0.22 g. 2-methylamino-4-hydroxy-6,7-dimethylpteridine (XV), fine light yellow needles from water, m. 277-81°. The filtrate from 1 g. XV and 0.57 g. BaCl2 added to 1 g. Bz2 in 25 cc. alc., and the mixt. refluxed 2 hrs. yielded 2-methylamino-4-hydroxy-6,7-diphenylpteridine (XVI), decomp. 346-54°. XVI (0.175 g.), 10 cc. POCl3, and 0.7 g. PCl5 refluxed 2 hrs., the POCl3 distd. off, and the residue poured onto ice yielded chlorinated XVI (XVII). XVII (1 g.) and 20 cc. MeOH (satd. with NH3 at 0°) heated in a sealed tube 16 hrs. at 155° yielded 2,4-diamino-6,7-diphenylpteridine. XIV (8.4 g.) with IV and V yielded N-(p-[(2-methylamino-4-hydroxy-6-pteridylmethyl)amino]benzoyl)glutamic acid. XI (8 g.) yielded 7.2 g. sulfate. XI (25 g.) dissolved in 2.5 l. water with dil. NaOH, 28 g. NaNO2 added, then AcOH slowly, and the ppt. in 3 l. water heated to 100° yielded 10.2 g. bluish red 3-methyl-2,6-diamino-5-nitroso-4(3H)-pyrimidone (XVII). IIA (20 g.) added to 10 g. XVII dissolved in 300 cc. water with a min. of dil. NaOH at 60° yielded 5.1 g. 3-methyl-2,5,6-triamino-4(3H)-pyrimidone (XVIII). XVIII (2 g.) in 75 cc. water at 40° with 1 g. Ac2 yielded 1.1 g. 2-amino-3,6,7-trimethyl-4(3H)-pteridinone, began to sublime at 350-60°, did not m. below 370°.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- (preparation of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

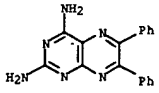


L8 ANSWER 33 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

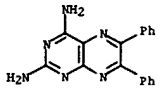


L8 ANSWER 33 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1951:61112 CAPLUS
DOCUMENT NUMBER: 45:61112
ORIGINAL REFERENCE NO.: 45:10388d-h
TITLE: Chemotherapy of cholera. V. Effects of oral administration of pteridines, sulfonamides, and their mixtures to mice
AUTHOR(S): Collier, H. O. J.; Hall, Iris F.
CORPORATE SOURCE: Allen & Hanbury, Ltd., Ware, UK
SOURCE: Annals of Tropical Medicine & Parasitology (1951), 45, 51-7
CODEN: ATMPA2; ISSN: 0003-4983
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 45, 5815i. 2,4-Diamino-6,7-diisopropylpteridine (I), 2,4-diamino-10-methyl-10H-indolo[3,2-g]pteridine (II), and 2,4-diamino-6,7-bis(p-methoxyphenyl)pteridine (III) were tested for acute oral toxicity to mice and were also fed to mice in the diet, alone or with sulfaguanidine (IV). For oral toxicity tests the pteridines were prepared in 10% gum acacia and given by stomach tube. The LD50, in mg./kg., of I was 966 and of II was > 5000. Mice receiving I showed convulsions. All 3 pteridines retarded the growth of mice fed 0.2-0.8% of the compound in the diet for 21 days. Growth was resumed when the animals were returned to the stock diet. Mortality was low from feeding I and II, but was up to 100% of the mice at the 0.8% level of III. Feces collected from the mice on the feeding test were assayed for vibriostatic activity by the fecal-suspension method (cf. C.A. 44, 6521d). The vibriostatic titer (V.T.) (i.e., the maximum number of dilns. necessary before a fecal suspension loses all vibriostatic activity) of 4% of IV in the diet was 160-320, tested against an inoculum of 103 vibrios of Vibrio cholerae per ml., for 24 hrs. Under the same conditions the V.T. of 0.2, 0.4, and 0.8% dietary levels of I and II was, resp., <80, <80, and 80; 320, 320-640, and 5120; and <80 for all levels of III. Feces from diets containing 0.4% pteridine plus 3.6% of IV showed a V.T. of 1280, 2560, and 320 for I, II, and III, resp. The percentage of dry weight of the compds. in the feces was 0.3 and 0.9% for I at the low and high diet level; 0.1 and 1.0% for II; and 0.3 and 1.5% for III. The pteridines were estimated fluorometrically. Although chloroamphenicol (V) was powerfully vibriostatic in vitro when added to normal mouse fecal suspensions (min. vibriostatic concentration 0.5 γ/ml.), there was no vibriostatic activity seen in the feces of mice fed 1.0% of V in the diet. For I, II, III, and IV, resp., the in vitro activities were, in γ/ml., 15.5, 2.0, > 500, and 500; and 7.8 and 3.9 for I- and II-phosphates, resp.
IT 694514-86-8, Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)- (toxicity of)
RN 694514-86-8 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)- (5CI) (CA INDEX NAME)

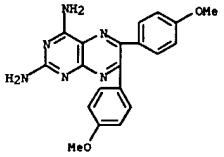
L8 ANSWER 34 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1951:45059 CAPLUS
DOCUMENT NUMBER: 45:45059
ORIGINAL REFERENCE NO.: 45:7691h
TITLE: Effect of 2,4-diamino-5-(p-chlorophenoxy)-6-methylpyrimidine and 2,4-diamino-6,7-diphenylpteridine on a chloroguanide-resistant strain of Plasmodium gallinaceum
AUTHOR(S): Greenberg, Joseph; Richeson, Edna M.
CORPORATE SOURCE: Natl. Inst. Health, Bethesda, MD
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1951), 77, 174-6
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB A chloroguanide-resistant strain of Pl. gallinaceum was cross-resistant to the second compound but not to the first. The first compound and chloroguanide were not synergistic in their antimalarial activity.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl- (effect on chloroguanide-resistant Plasmodium pallinaceum)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



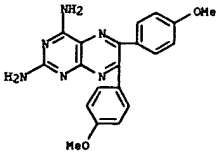
L8 ANSWER 35 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1951:33453 CAPLUS
DOCUMENT NUMBER: 45:33453
ORIGINAL REFERENCE NO.: 45:5816e-h
TITLE: Chemotherapy of cholera. IV. Antagonism of the antibacterial activities of 2,4-diaminopteridines, sulfaguanidine, and their mixtures
AUTHOR(S): Collier, H. O. J.; Waterhouse, Pamela D.
CORPORATE SOURCE: Allen and Hanburys, Ltd., Ware, UK
SOURCE: Annals of Tropical Medicine & Parasitology (1950), 44, 273-80
CODEN: ATMPA2; ISSN: 0003-4983
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The antagonism was examined of pteroylglutamic acid (PGA), pteroic acid (PA), p-aminobenzoic acid (PABA), and peptone towards the bacteriostatic and vibriostatic activities of 2,4-diamino-6,7-diethyl (I), diisopropyl (II), and diphenyl (III) pteridines, and 2,4-diamino-1'-methylindolo-(2',3',6,7-)pteridine (IV), and 4-aminopteroylglutamic acid (V). Streptococcus faecalis, which is unable to synthesize the pteridine moiety, and V. cholerae were used. Against S. faecalis II and IV were more active than I, and their inhibitory effects were less readily overcome by PGA. III and V were roughly 10% as active as IV, at the levels of PGA used (0.002 to 0.2 γ/ml.). The ratio of inhibitor to PGA at the concentration producing 50% inhibition was not constant, falling with increasing PGA concns. in the case of pteridines II, III, IV, and V, but rising for I. Some antagonism towards II and IV was shown by PA at 0.02 to 2 γ/ml. With V. cholerae 100 γ/ml. of PGA overcame to some extent the inhibitory activity of the pteridines and of sulfaguanidine (VI), alone or in combination. Ten γ/ml. of PGA had no effect. PA at 100 γ/ml. also overcame the vibriostatic action of II and IV; but 1 γ/ml. was ineffective. PABA (0.001 to 0.1 γ/ml.) did not antagonize the activity of the pteridines, but was effective against VI. Peptone, at 100 γ/ml. readily antagonized the vibriostatic action of VI, and to a lesser extent that of II, but had no effect on action of IV.
IT **18181-93-6**, Pteridine, 2,4-diamino-6,7-diphenyl-
(in cholera therapy)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



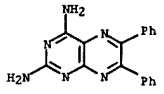
L8 ANSWER 36 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1951:33452 CAPLUS
DOCUMENT NUMBER: 45:33452
ORIGINAL REFERENCE NO.: 45:5816c-e
TITLE: Chemotherapy of cholera. III. The action of pteridine-sulfonamide mixtures upon Vibrio cholerae and upon the mouse
AUTHOR(S): Collier, H. O. J.; Hall, Iris F.; Waterhouse, Pamela D.
CORPORATE SOURCE: Allen and Hanburys, Ltd., Ware, UK
SOURCE: Annals of Tropical Medicine & Parasitology (1950), 44, 161-7
CODEN: ATMPA2; ISSN: 0003-4983
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The 2,4-diamino-6,7-diethyl, dipropyl, diisopropyl (I), di-sec-butyl, di(1-furyl), and di(p-methoxyphenyl) (II) pteridines, 2,4-diaminocamphano-(2',3',6,7 or 7,6)pteridine, and 2,4-diamino-1'-methylindolo-(2',3',6,7)-pteridine (III) were tested with and without sulfaguanidine (IV). All showed marked synergism with IV. A mixture composed of 10% pteridine and 90% IV had about the same activity as the pure pteridine for incubation periods up to 24 hrs. The mixts. were generally more active than the pure pteridines upon longer incubation. The LD50 (in mg./kg., intraperitoneally in mice) of I, II, and III, resp., was: 141, 186, and 126; the LD50 of IV was 870. The LD50 of 10% mixts. of I, II, and III with IV were, resp., 1023, 890, and 578 mg./kg.
IT **694514-86-8**, Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)-
(in cholera therapy)
RN 694514-86-8 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)- (5CI) (CA INDEX NAME)



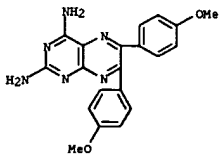
L8 ANSWER 37 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1951:33451 CAPLUS
DOCUMENT NUMBER: 45:33451
ORIGINAL REFERENCE NO.: 45:5815i,5816a-c
TITLE: Chemotherapy of cholera. II. In vitro vibriostatic properties of certain 2,4-diaminopteridines
AUTHOR(S): Collier, H. O. J.; Waterhouse, Pamela D.
CORPORATE SOURCE: Allen and Hanburys, Ltd., Ware, UK
SOURCE: Annals of Tropical Medicine & Parasitology (1950), 44, 156-60
CODEN: ATMPA2; ISSN: 0003-4983
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 44, 6521d. 6,7-Disubstituted 2,4-diaminopteridines were prepared and tested for vibriostatic activity. Of the 2,4-diamino-6,7-dialkylpteridines the diisopropyl (I) and di-sec-Bu (II) compds. were the most active but the di-Et and di-Pr derivs. were also active. Generally, alkyl substituents of less than 2 or more than 3 C atoms were inactive. In the 6,7-diaryl series di(p-methoxyphenyl) and di(1-furyl) derivs. were active but the di(o-methoxyphenyl), di-Ph, and dibenzyl compds. were not. With condensed ring substituents at the 6,7-positions, the most effective was 2,4-diamino-1'-methylindolo-(2',3',6,7)pteridine (III). In all other compds. tested the min. inhibitory concentration rose markedly as the incubation time increased. The 1'-Et and 1'-propylindolo-(2',3',6,7) compds. were active at about 20-40 γ/mL. Sulfaguanidine (IV) was used for comparison. Only III remained fully as effective against 106 as against 103 vibrios/mL. All strains of vibrios tested were inhibited by III. There was no difference in activity of I in a synthetic medium as compared to a peptone broth, while the min. inhibitory concentration of IV was lower in the synthetic medium. The phosphate, Cl-, and NO3- salts of III were prepared and tested at various pH values in the synthetic medium. The phosphate showed good activity from pH 7 to 8.5, the growth range for vibrios. The solubilities in H2O at 37° and pH 7 of several of the compds. (in mg./mL.) were: I, 0.1; I-phosphate, 18.7; II, 0.12; II-phosphate, 27.7; III, 0.04; and III-phosphate, 0.58.
IT **694514-86-8**, Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)-
(in cholera therapy)
RN 694514-86-8 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)- (5CI) (CA INDEX NAME)



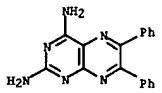
L8 ANSWER 38 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1950:43971 CAPLUS
DOCUMENT NUMBER: 44:43971
ORIGINAL REFERENCE NO.: 44:8417b-c
TITLE: Vibriostatic activity in certain series of pteridines
AUTHOR(S): Collier, H. O. J.; Campbell, N. R.; Fitzgerald, M. E. H.
CORPORATE SOURCE: Allen & Hanburys, Ltd., Ware, Herts, UK
SOURCE: Nature (London, United Kingdom) (1950), 165, 1004-5
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Condensations of tetraminopyrimidine with N-methylisatin in the presence of mineral acid gives a mixture of an active vibriostatic isomer 2, 4-diamino-1'-methylindole-(2', 3', 6, 7)-pteridine. In tests. (against Vibrio cholerae) the activity was greatest in the diisopropyl compound
IT **18181-93-6**, Pteridine, 2,4-diamino-6,7-diphenyl-
694514-86-8, Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)-
(vibriostatic activity of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



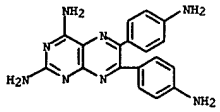
RN 694514-86-8 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis(p-methoxyphenyl)- (5CI) (CA INDEX NAME)



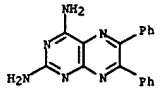
L8 ANSWER 39 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1950:28053 CAPLUS
DOCUMENT NUMBER: 44:28053
ORIGINAL REFERENCE NO.: 44:5480c-f
TITLE: Antimalarial activity of 2,4-diamino-6,7-diphenylpteridine; its potentiation by sulfadiazine and inhibition by pteroylglutamic acid
AUTHOR(S): Greenberg, Joseph
CORPORATE SOURCE: Natl. Inst. Health, Bethesda, MD
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1949), 97(No. 4, Pt. I), 484-7
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB 2,4-Diamino-6,7-dimethylpteridine (DR 15,789), 2,4-diamino-6,7-dicarboxypteridine (DR 15,790), 2,4-diamino-6,7-diphenylpteridine (DR 15,791), 2-amino-4-hydroxy-6,7-dimethylpteridine (DR 15,793), 2-amino-4-hydroxy-6,7-diphenylpteridine (DR 15,792), and 2,4-diamino-6,7-bis(p-aminophenyl)-pteridine (DR 15,794) were tested for antimalarial activity against Plasmodium gallinaceum in chicks. Only DR 15,791 was able to suppress parasitemia at doses tolerated by the chick. Its antimalarial activity was about equal to that of quinine. Its action was markedly potentiated in vivo by sulfadiazine and significantly, but not completely, inhibited by pteroylglutamic acid. DR 15,794 and DR 15,789 had some antimalarial activity when administered with subeffective doses of sulfadiazine. DR 15,789 was much more toxic than the other compds.
IT **18181-93-6**, Pteridine, 2,4-diamino-6,7-diphenyl-
151648-52-1, Pteridine, 2,4-diamino-6,7-bis(p-aminophenyl)-
(antimalarial activity of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



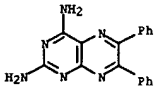
RN 151648-52-1 CAPLUS
CN 2,4-Pteridinediamine, 6,7-bis(4-aminophenyl)- (9CI) (CA INDEX NAME)



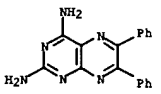
L8 ANSWER 39 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
IT **18181-93-6**, Pteridine, 2,4-diamino-6,7-diphenyl-
(antimalarial activity of, and its potentiation by sulfadiazine and inhibition by folic acid)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



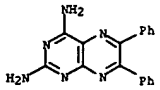
L8 ANSWER 40 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1950:14970 CAPLUS
DOCUMENT NUMBER: 44:14970
ORIGINAL REFERENCE NO.: 44:2992b-d
TITLE: A new synthesis of pteridines
AUTHOR(S): Timmis, G. M.
SOURCE: Nature (London, United Kingdom) (1949), 164, 139
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB Isomer formation and ambiguity about the structure of the product arising from the condensation of 4,5-diaminopyrimidines with diketones or other suitable compds. are avoided by using 5-nitroso-4-aminopyrimidines and ketones as reactants. The following derivs. of I have been made by condensation in HOAc at 100-60°. R1, R2 = NH2, R3, R4 = Ph, m. 282°; R1, R2 = NH2, R3 = Ph, R4 = Me, m. 330°; R1, R2 = NH2, R3 R4 = -CO.NH.CO.NH-, absorption maximum, λ 264, 369 (log .vepsiln. 4.11, 4.34), min., λ 294 (log .vepsiln. 3.59); and R1, R2 = OH, R3R4 = -CO.NH.CO.NH-, absorption maximum, λ 280, 388 (log .vepsiln. 4.2, 4.3), min., λ 275, 322 (log .vepsiln. 4.16, 3.4).
IT **18181-93-6**, Pteridine, 2,4-diamino-6,7-diphenyl-
(preparation of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 41 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1949:47440 CAPLUS
DOCUMENT NUMBER: 43:47440
ORIGINAL REFERENCE NO.: 43:8555e-h
TITLE: Hematologic effect in rats of pterins structurally related to pteroylglutamic acid
AUTHOR(S): Swendseid, Marian E.; Wittle, E. L.; Moersch, G. W.; Bird, O. D.; Brown, Raymond A.
SOURCE: Journal of Biological Chemistry (1949), 179, 1175-82
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The compds. studied were 2,4-diamino-6,7-diphenylpteridine (I), 2,4-diamino-6,7-dimethylpteridine (II), 2-amino-4-hydroxy-6,7-diphenylpteridine (III), 4-aminopteroylglutamic acid (IV), and crude 4-desoxypteroylglutamic acid (V). I, II, and III inhibited the growth of S. faecalis at a much lower level than L. casei; IV and V inhibited both organisms at similar levels. Weanling rats receiving diets containing 50 mg. of I/100 g. developed leucopenia with agranulocytosis, but there was no effect on hemoglobin concentration. The leucopenia was prevented by the addition of an equivalent amount of pteroylglutamic acid (VI). II and III, at 50 mg. %, had no effect on hematologic pattern, but II at 500 mg. % gave results similar to those with I. IV caused leucopenia with agranulocytosis and also anemia when fed at a level of 0.3 mg. %. The changes were prevented by the addition of an equivalent amount of VI. The effect of V was similar to that of IV, but the dietary level required was much higher (500 mg. %). II and V, at lower levels, prevented the agranulocytosis caused by the feeding of sulfasuxidine.
IT **18181-93-6**, Pteridine, 2,4-diamino-6,7-diphenyl-
(hematologic effect of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

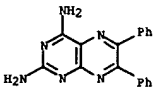


L8 ANSWER 42 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1949:47037 CAPLUS
DOCUMENT NUMBER: 43:47037
ORIGINAL REFERENCE NO.: 43:8491c-e
TITLE: Quantitative interference with estrogen-induced tissue growth by folic acid antagonists
AUTHOR(S): Hertz, Roy; Tullner, Wm. W.
SOURCE: Endocrinology (1949), 44, 278-82
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 42, 4659a. In stilbestrol-treated chicks and estradioltreated ovariectomized rats, quant. inhibition of estrogen-induced tissue growth in the female genital tract was obtained with the folic acid antagonists, 4-aminopteroylaspartic, 4-desoxypteroylglutamic, and 4-amino-N10-methylpteroylglutamic acids, 2,4-diamino-6,7-dimethylpteridine, 2,4-diamino-6,7-diphenylpteridine, 2-amino-4-hydroxy-6,7-diphenylpteridine, and 2-amino-4-hydroxy-6,7-bis(p-aminophenyl)pteridine. The inhibition was reversed by administration of folic acid.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl-
(effect on estrogen-induced tissue growth)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)

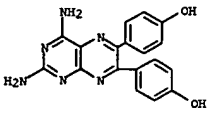


L8 ANSWER 43 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1949:22617 CAPLUS
DOCUMENT NUMBER: 43:22617
ORIGINAL REFERENCE NO.: 43:4268e-i,4269a-c
TITLE: Pteridines. IV. Derivatives of 2,4-diamino-6,7-diphenylpteridine
AUTHOR(S): Cain, C. K.; Taylor, E. C., Jr.; Daniel, Louise J.
SOURCE: Journal of the American Chemical Society (1949), 71, 892-6
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 43, 654d. 2,4-Diamino-6,7-diphenylpteridine (I) (1 g.) and 50 mL. Ac2O, refluxed 16 h., give 55% of the N4-Ac derivative, light yellow, m. slowly at 140-50°; 0.5 g. I, 10 mL. Ac2O, and 3 mL. H2SO4, heated 1 h. on the steam bath, give 68% of the N2,N4-di-Ac derivative, light yellow, decompose slowly above 190°. 2-Amino-4-hydroxy-6,7-diphenylpteridine (II) (1 g.), 60 mL. POCl3, and 5 g. PCl5, refluxed 2 h., give 81% of the 4-Cl compound (III), bright yellow, could not be crystallized because of hydrolysis to II. III (1 g.), 10 mL. MeNH2, and 30 mL. EtOH, heated 16 h. at 155°, give 27% 2-amino-4-methylamino-6,7-diphenylpteridine, bright yellow, m. 237-8° (corrected). 2,4,5,6-Tetraaminopyrimidine sulfate (2 g.) in 90 mL. H2O, treated with 2 g. (p-H2NC6H4CO)2.H2SO4 and refluxed 1 h., gives 1.73 g. 2,4-diamino-6,7-bis(p-aminophenyl)pteridine (IV), bright orange, decompose 308-9° (corrected). 2,4,5,6-Tetraaminopyrimidine (V) (1.1 g.) in 75 mL. H2O and 1.35 g. (p-AcNHC6H4CO)2 in 100 mL. EtOH, refluxed 7 h., give 82% of the di-Ac derivative of IV, m. 234-7° (corrected). IV (0.1 g.) in 4 mL. boiling H2O containing sufficient concentrated HCl to cause solution, treated with 0.2 mL. 40% HCHO and adjusted to pH 7.5 with NaHCO3, gives a quant. yield of 2,4-diamino-6,7-bis(p-[(hydroxymethyl)amino]phenyl)pteridine (VI), does not m. below 300°. VI and NaHSO3 in H2O, refluxed 3 h., give 88% of the p-[(sulfitomethyl)amino]phenyl compound (di-Na salt), does not m. below 300°; HC(OH)SO3Na gives 76% of the p-[(sulfinomethyl)amino]phenyl compound (VII) as the di-Na salt which does not m. at 300°. IV (0.2 g.), 3.2ml. Ac2O, and 1.9ml. AcOH, heated 45 min. at 80°, give 56% 2,4-diacetamido-6,7-bis(p-acetamidophenyl)pteridine, with 1 mol. H2O, light yellow. IV (0.2 g.) in 7 mL. H2O and 0.8 mL. concentrated H2SO4, treated with NaNO2, heated 15 min. at 60°, and 1 h. at 100°, gives 71% 2,4-diamino-6,7-bis(p-hydroxyphenyl)pteridine, yellow; it was prepared also from (p-HOC6H4CO)2 and the bisulfite (VIII) of V (84%). V (3 g.) and 2 g. (m-O2NC6H4CO)2 in 70 mL. EtOH and 15 mL. AcEt, refluxed 3 h., give a quant. yield of 2,4-diamino-6,7-bis(m-nitrophenyl)pteridine, m. 307-8° (corrected); catalytic reduction gives 65% of the m-aminophenyl compound, orange-yellow, decompose above 180°. The m-isomer of VII (85% yield) is hygroscopic and rapidly forms a trihydrate in the air. VIII (5 g.) in 20 mL. 0.5% NaOH, added to 5 g. phenanthrenequinone-3-sulfonic acid in 130 mL. H2O and refluxed 30 min., gives 88% 2,4-diaminophenanthro[9,10-e]pteridine-8(or 11)-sulfonic acid, light yellow, does not m. up to 360°. The absorption spectra of these compds., qual. solubility in H2O, EtOH, and 0.1 N HCl and NaOH, and their inhibitory indexes against Streptococcus faecalis are given. A (sulfinomethyl)amino group confers H2O solubility with the

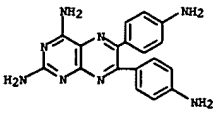
L8 ANSWER 43 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
retention of antifolic acid activity. The introduction into I of any of the solubilizing groups investigated results in some lowering of antifolic acid activity; the effect of certain structural changes in I on such activity is discussed.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl-
(and derivs.)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



IT 6967-77-7, Pteridine, 2,4-diamino-6,7-bis(p-hydroxyphenyl)-
151648-52-1, Pteridine, 2,4-diamino-6,7-bis[p-aminophenyl)-
804555-05-3, Acetanilide, 4'-[7-(p-acetamidophenyl)-2,4-diamino-6-pteridyl]- 855629-16-2, Phenol, p-[2,4-diamino-7-[o-hydroxyphenyl]-6-pteridyl]- 855868-52-9, Methanol, [p-[2,4-diamino-7-[p-[(hydroxymethyl)amino]phenyl]-6-pteridyl]anilino]-
857228-86-5, Pteridine, 2,4-diamino-6,7-bis[m-aminophenyl]-
857398-11-9, Pteridine, 2,4-diamino-6,7-bis(m-nitrophenyl)-
(preparation of)
RN 6967-77-7 CAPLUS
CN Phenol, 4,4'-(2,4-diamino-6,7-pteridinediyl)bis- (9CI) (CA INDEX NAME)

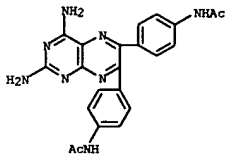


RN 151648-52-1 CAPLUS
CN 2,4-Pteridinediamine, 6,7-bis(4-aminophenyl)- (9CI) (CA INDEX NAME)

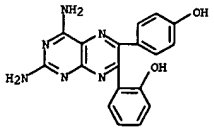


RN 804555-05-3 CAPLUS
CN Acetanilide, 4'-[7-(p-acetamidophenyl)-2,4-diamino-6-pteridyl]- (5CI) (CA INDEX NAME)

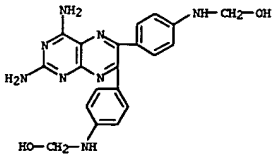
L8 ANSWER 43 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 855629-16-2 CAPLUS
CN Phenol, p-[2,4-diamino-7-[o-hydroxyphenyl]-6-pteridyl]- (5CI) (CA INDEX NAME)

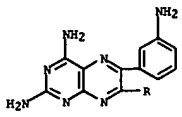


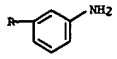
RN 855868-52-9 CAPLUS
CN Methanol, [p-[2,4-diamino-7-[p-[(hydroxymethyl)amino]phenyl]-6-pteridyl]anilino]- (5CI) (CA INDEX NAME)



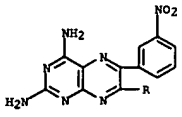
RN 857228-86-5 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis[m-aminophenyl]- (5CI) (CA INDEX NAME)

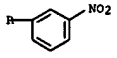
L8 ANSWER 43 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



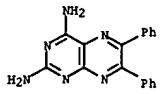


RN 857398-11-9 CAPLUS
CN Pteridine, 2,4-diamino-6,7-bis[m-nitrophenyl]- (5CI) (CA INDEX NAME)

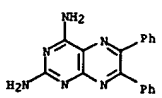




L8 ANSWER 44 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1947:37525 CAPLUS
DOCUMENT NUMBER: 41:37525
ORIGINAL REFERENCE NO.: 41:7438i,7439a-b
TITLE: Growth inhibition of bacteria by synthetic pterins. I. Studies with Streptococcus faecalis, Lactobacillus casei, and Lactobacillus arabinosus
AUTHOR(S): Daniel, Louise J.; Norris, L. C.; Scott, M. L.; Heuser, G. F.
CORPORATE SOURCE: Cornell Univ., Ithaca
SOURCE: Journal of Biological Chemistry (1947), 169, 689-97
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The following synthetic pterins were used: 2,4-diamino-6,7-dimethylpyrimido-(4,5-b)pyrazine, 2,4-diamino-7-methylpyrimido(4,5-b)pyrazine, 2,4-diamino-6,7-dicarboxypyrimido(4,5-b)pyrazine, 2,4-diamino-7-carboxypyrimido-(4,5-b)pyrazine, 2,4-diamino-6,7-diphenylpyrimido(4,5-b)pyrazine, 2,4-diaminopyrimido(4,5-b)pyrazine, 2,4-diaminophenanthro(9,10-e)pyrimido(4,5-b)pyrazine, 2,4-diaminoacenaphtho(1,2-e)pyrimido(4,5-b)pyrazine. Certain of these possess high antibacterial activity, not only for S. faecalis and L. casei which require folic acid (I) as an essential nutrient, but also for L. arabinosus, which synthesizes its own I. The substitution of OH for NH2 in the 4- or 2-position destroyed the anti-I activity. Those pterins with 4-NH2 groups varied in anti-I with the nature of the substitution in the 6- and 7-positions.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl-
(growth inhibition of bacteria by)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 45 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1947:31103 CAPLUS
DOCUMENT NUMBER: 41:31103
ORIGINAL REFERENCE NO.: 41:6258a-f
TITLE: Pyrimido[4,5-b]pyrazines. II. 2,4-Diaminopyrimido[4,5-b]pyrazine and derivatives
AUTHOR(S): Mallette, M. F.; Taylor, E. C., Jr.; Cain, C. K.
CORPORATE SOURCE: Cornell Univ., Ithaca, NY
SOURCE: Journal of the American Chemical Society (1947), 69, 1814-16
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 41:31103
GI For diagram(s), see printed CA Issue.
AB cf. C.A. 41, 135f. A modification is given of Traube's method (Ber. 37, 4544(1904)) for the preparation of H2NC:C(NH2).N: C(NH2).N:CNH2 from CH2(CN)2 and NH:C(NH2)2 in 54% yield (as the bisulfite compound (I)). I (15 g.) and 20 g. (CHO.NaHSO3)2 in 250 ml. H2O, heated to boiling, acidified to pH 3 with dilute HCl, and boiled 20 min., give 88% 2,4-diaminopyrimidino[4,5-b]pyrazine (II), needles, HC:N.C.N:CNH2 HC:N.C.C(NH2): N (II) decompose on heating; this and some of its derivs. could not be analyzed by ordinary combustion procedures. I (50 g.), 20 ml. Ac2, and 300 ml. H2O, heated 1 hr. at 80°, give 85% of the 6,7-di-Me derivative of II, prisms, decompose on heating. I (5 g.), 5 g. Bz2, 3 ml. concentrated HCl, 50 ml. EtOH, 50 ml. EtAc, and 100 ml. H2O, refluxed 2 hrs., the pH adjusted to 6, and the product crystallized from 80% HCO2H, give 84% of the 6,7-di-Ph derivative of II, m. 280-3° (decomposition). I (4.5 g.) in 50 ml. H2O and 5 ml. concentrated HCl, treated with 1 g. acenaphthenequinone in 25 ml. HCONMe2 and the mixture heated 4 hrs. on the steam bath, give 90,% 2,4-diaminoacenaphtho[1,2-e]pyrimido[4,5-b]pyrazine, needles, decompose on heating. I (2 g.), 1.5 g. phenanthreneqvinone, 250 ml. 95% EtOH, and 5 ml. 10% aqueous NaOH, refluxed 6 hrs., give 84% 2,4-diaminophenanthro[9,10-e]pyrimido[4,5-b]pyrazine, needles, sinters 340° without melting. I (15 g.), 6 g. AcCHO, and 200 cc. H2O give 90% of the 6(or 7)-Me derivative of II, prisms, decompose on heating. All these compds. show parallel extinction. The ultraviolet absorption spectra are given of the above compds. and of some reported in Part I. Several derivs. of II exhibit marked antifolic acid activity for several bacteria.
IT 18181-93-6, Pteridine, 2,4-diamino-6,7-diphenyl-
(preparation of)
RN 18181-93-6 CAPLUS
CN 2,4-Pteridinediamine, 6,7-diphenyl- (9CI) (CA INDEX NAME)



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